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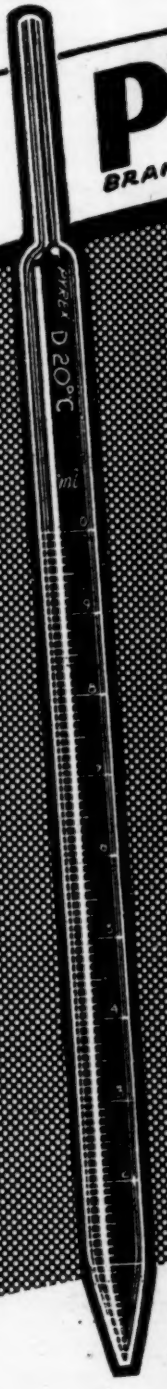

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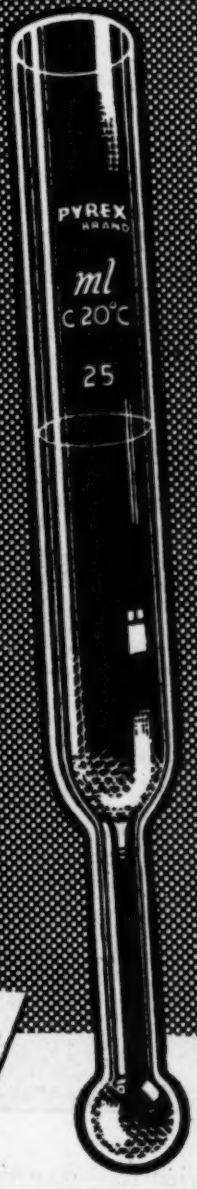

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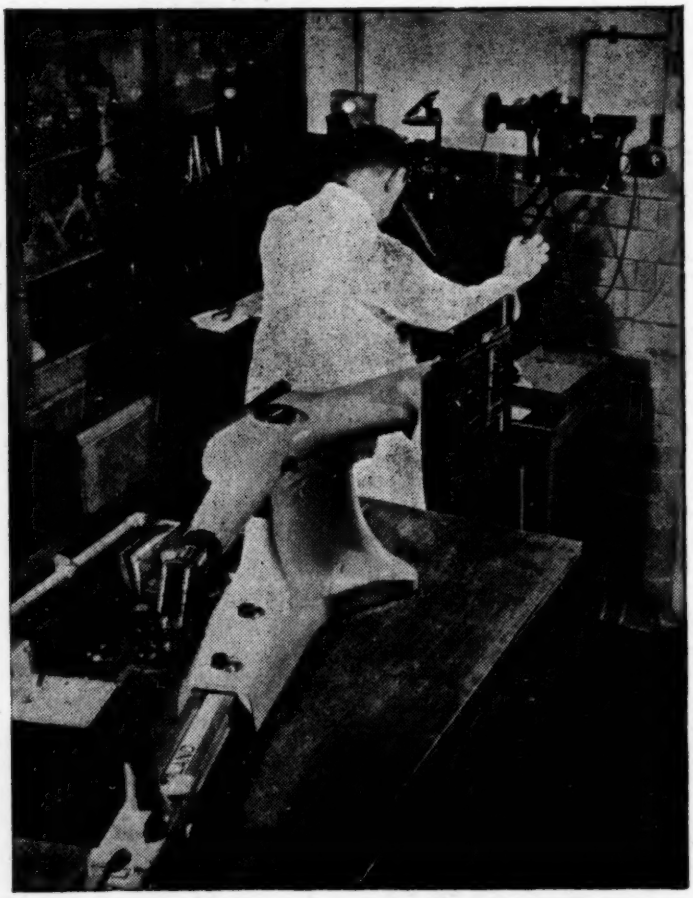

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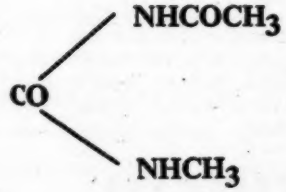

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TABLE I.

Substance.	$d_4^{25°}$.	$d_4^{100°}$.	$\gamma^{25°}$.	$\gamma^{100°}$.	$n_{4358}^{25°}$.	$n_{4861}^{25°}$.	$n_{5461}^{25°}$.	$n_D^{25°}$.	$n_{6563}^{25°}$.
Benzene	0·87368	—	—	—	1·51979	1·50987	1·50210	1·49818	1·49340
m-Xylene	0·86010	—	—	—	1·5154	1·5061	1·4987	1·4949	1·4906
Dimethylaniline	0·95241	—	—	—	1·5900	1·5741	1·5621	1·5562	1·5496
m-2-Xylidine	0·97763	—	37·91	—	1·58662	1·57434	1·56369	1·55855	1·55273
m-4-Xylidine *	0·97185	—	36·49	—	1·5856	1·5725	1·5622	1·5570	1·5512
m-5-Xylidine	0·97038	—	36·38	—	1·58470	1·57150	1·56153	1·55635	1·55047
Dimethyl-*m*-2-xylidine	0·91507	0·8493	29·74	24·06	1·53552	1·52640	1·51762	1·51365	1·50920
Dimethyl-*m*-4-xylidine	0·91269	0·8474	30·88	24·15	1·54032	1·53070	1·52230	1·51808	1·51325
Dimethyl-*m*-5-xylidine	0·92751	0·8651	35·17	26·73	1·57272	1·55659	1·54772	1·54236	1·53631

* Buehler, Wood, Hull, and Erwin (*J. Amer. Chem. Soc.*, 1932, **54**, 2398) give $d^{25°}$ 0·9723, $\gamma^{25°}$ 36·75.

TABLE II.

Substance.	$[P]^{25°}$.	$[P]^{100°}$.	$[R_L]_{4358}$.	$[R_L]_{4861}$.	$[R_L]_{5461}$.	$[R_L]_D$.	$[R_L]_{6563}$.	M.S.V.
Benzene	—	—	27·14	26·64	26·36	26·17	25·97	—
Dimethylaniline	—	—	42·88	41·93	41·21	40·85	40·45	—
m-Xylene	—	—	37·19	36·62	36·17	35·93	35·67	—
m-2-Xylidine	307·1	—	41·57	40·86	40·24	39·94	39·59	—
				(40·90) [1]		(40·01) [1]	(39·66) [1]	
m-4-Xylidine	306 [2]	—	41·76	40·99	40·39	40·08	39·74	—
						(40·04) [3]	(39·68) [3]	
m-5-Xylidine	306·2	—	41·77	41·00	40·41	40·10	39·75	—
Dimethyl-*m*-2-xylidine	380·2	388·4	50·73	50·01	49·31	48·99	48·64	164·0
				(49·96) [1]		(49·01) [1]	(48·65) [1]	
Dimethyl-*m*-4-xylidine	384·8	389·8	51·32	50·56	49·90	49·55	49·17	164·2
				(50·49) [1]		(49·48) [1]	(49·13) [1]	
Dimethyl-*m*-5-xylidine	391·2	391·3	52·91	51·68	51·01	50·58	50·11	161·8

[1] Ley and Pfeiffer (*loc. cit.*). [2] Buehler, Wood, Hull, and Erwin (*loc. cit.*) give 307·2. [3] Brühl (*Z. physikal. Chem.*, 1895, **16**, 218).

dimethylation the position is reversed, *N*-dimethyl-*m*-2- having a lower density and lower refractive indexes than *N*-dimethyl-*m*-4-xylidine. The present density measurements agree with this conclusion in regard to *m*-2- and *m*-4-xylidine but not in regard to their dimethyl compounds. If we consider the difference of density between the xylidine and its *N*-dimethyl derivative we have the series *m*-5 < *m*-4 < *m*-2, *i.e.*, dimethylation of the vicinal xylidine results in the greatest lowering of density. The change in b. p. on dimethylation shows a similar regularity; whereas dimethylation *raises* the b. p. of aniline and of *m*-5-xylidine by 9° and 6°, respectively, it *lowers* the b. p. of *m*-4- and of *m*-2-xylidine by 9° and 22°, respectively. Such behaviour seems general: whenever a methyl group occupies a position ortho to the amino-group, dimethylation of the amine results in a lowering of b. p., whereas if the ortho-positions are unsubstituted a rise of b. p. results: *o*-toluidine (− 13°), *m*-toluidine (+ 8°), *p*-toluidine (+ 11°), *p*-xylidine (− 10°), *o*-xylidine (− 22°), mesidine (− 14°).

For each wave-length for which measurements have been made, the refractive indexes of the *m*-xylidines show only differences in the third decimal figure between the isomers, but they increase in the order *m*-5 < *m*-4 < *m*-2. On dimethylation the differences become greater (now affecting the second decimal figure); the order is reversed and becomes *m*-5 > *m*-4 > *m*-2. The molecular refractivities of *m*-5- and *m*-4-xylidines are indistinguishable; the value for *m*-2-xylidine is a little lower. The values for the dimethylxylidines are best discussed by reference to Table III, from which it is evident that the molecular refractivity of dimethyl-*m*-5-xylidine is normal as compared with dimethylaniline and dimethyl-*m*- and -*p*-toluidines, that whenever methyl or chlorine is substituted ortho to the dimethylamino-group it results in a reduction of approximately 1 c.c. in molecular refractivity, and that when both ortho-positions are occupied by methyl groups the molecular refractivity is lowered by about 1·6 c.c.

TABLE III.

	$[R_L]_D$.	Δ.		$[R_L]_D$.	Δ.
Dimethylaniline	40·85	14·68	Dimethyl-*p*-toluidine [1]	45·68	14·62
Benzene	26·17		Toluene [2]	31·06	
Dimethyl-*m*-5-xylidine	50·58	14·65	Dimethyl-*m*-toluidine [1]	45·68	14·62
m-Xylene	35·93		Toluene [2]	31·06	
Dimethyl-*m*-4-xylidine	49·55	13·62	Dimethyl-*o*-toluidine [1]	44·62	13·56
m-Xylene	35·93		Toluene [2]	31·06	
Dimethyl-*m*-2-xylidine	48·99	13·06	Dimethyl-*o*-chloroaniline [1]	44·95	13·57
m-Xylene	35·93		Chlorobenzene [2]	31·38	

[1] Ley and Pfeiffer (*loc. cit.*). [2] Landolt-Börnstein, "Tabellen."

By calculation from Brühl's values of atomic refractivities the introduction of a dimethylamino-group into a hydrocarbon should result in a change of molecular refractivity in the aromatic series of 14·62 c.c., in the aliphatic series of 13·25 c.c.; from Eisenlohr's figures the value in the aliphatic series should be 12·78 c.c. The atomic refractivity of nitrogen in dimethyl-*m*-2-xylidine must therefore approach very closely the value for nitrogen in a tertiary aliphatic amine. Hampson's dipole-moment measurements (J., 1939, 981) have

indicated the almost complete suppression of the resonance of the dimethylamino-group by the vicinal methyl groups in dimethylmesidine and nitrodimethylaminodurene; the value 54·2 c.c. given by him for the molecular refractivity (λ 5461) of dimethylmesidine is in complete agreement with the results now recorded, for the difference between that value and the value of 41·06 c.c. for mesitylene (Part I) is 13·14 c.c., as compared with 14·85 c.c. for the difference between the molecular refractivities (λ 5461) of dimethylaniline and benzene and 13·14 c.c. for the difference between dimethyl-*m*-2-xylidine and *m*-xylene for the same wave-length. It is noteworthy that exaltation of molecular refractivity appears to be shown by *p*- (Marsden and Sutton, J., 1936, 599) and by *o*-nitrodimethylaniline (Ley and Pfeiffer, *loc. cit.*): it is well known that in *p*-nitrodimethylaniline, *p*-nitroaniline, and *o*-nitroaniline reinforcement of resonance effects leads to increased dipole moments.

There is an increase in molecular solution volume on passing from *N*-dimethyl-*m*-5- to *N*-dimethyl-*m*-4-xylidine, but the value for the latter is indistinguishable from that for *N*-dimethyl-*m*-2-xylidine. The values of molecular solution volume are practically identical with the values of M/d for the pure liquids at the same temperature.

The parachors of the three *m*-xylidines are practically identical (306—307) but considerably lower than the sum of the atomic parachors (314·6); this low value is confirmed by Buehler, Wood, Hull, and Erwin (*loc. cit.*), who found the parachor of *m*-4-xylidine to be 307·2. For the *N*-dimethyl-*m*-xylidines the sum of the atomic parachors is 392·7: *N*-dimethyl-*m*-5-xylidine (391·2) is practically normal, but the parachors of the three isomers decrease in the order *m*-5 > *m*-4 > *m*-2 (a sequence confirmed by measurements at 100°), thus reversing the sequence found in the dichloronitrobenzenes (cf. Part I). This contrasting behaviour raises the question of the physical conception of the parachor. Interpretation of it as a molecular volume has been adversely criticised by Ferguson (*Nature*, 1930, **125**, 597) and by Reilly and Rae ("Physico-chemical Methods," 3rd edn., 1940, vol. 1, p. 110), the latter contending that it cannot have the dimensions of volume since it is calculated by multiplying M/d (which has the dimensions of volume) by the fourth root of the surface tension (which is not dimensionless) measured at the same temperature as d. Now the molecular refractivity has undoubtedly the dimensions of volume: it is again M/d multiplied by a factor [in this case $(n^2 - 1)/(n^2 + 2)$], and the molecular solution volume when measured in benzene solution approximates closely to the value of M/d for the pure liquid at the same temperature; since the data for the dichloronitrobenzenes (cf. Part I) and the data now presented show that in a series of position isomers, although the molecular solution volume may increase, the molecular refractivity can decrease, there seems to be no reason why in such homologous series variations in the parachor should of necessity have always the same sign as variations in either of these other properties.

Experimental.

Refractive indexes were measured on a Hilger–Pulfrich refractometer, and surface tensions at 25° by Sugden's differential bubble-pressure method and at 100° by Ferguson's method (cf. Part I). In calculating the parachors the density of the saturated vapour has been neglected.

Materials.—*m*-Xylene, dimethylaniline, *m*-4- and *m*-2-xylidine were obtained by repeated fractionation of products supplied as these specific compounds by B.D.H. The b. p.'s of the fractions used were: *m*-xylene 139°, dimethylaniline 192·5°, *m*-4-xylidine 213·5—214°, *m*-2-xylidine 216·5—217°. The molecular refractivities are in good agreement with those recorded in the literature. *m*-5-Xylidine was prepared from *m*-4-xylidine by Haller and Adams's method (*J. Amer. Chem. Soc.*, 1920, **42**, 1840) and purified by crystallisation of the acetyl derivative. The fraction used boiled at 223°/774 mm.

The dimethylxylidines were prepared by methylation with methyl sulphate. Use of acetic anhydride to remove unchanged or monomethylated amine was unsatisfactory (since the *N*-acetomethyl-*m*-2- and -*m*-4-xylidides have b. p.'s very close to those of the *N*-dimethylxylidines), and in the methylation of *m*-2-xylidine it was replaced by *p*-toluenesulphonyl chloride. The *N*-dimethyl-*m*-2-xylidine had b. p. 194·5—195°/760 mm. (Found: C, 80·3; H, 9·9. Calc. for $C_{10}H_{15}N$: C, 80·5; H, 10·1%). For methylation of *m*-4- and *m*-5-xylidines the method of Evans and Williams (J., 1939, 1199) was adopted. *N*-Dimethyl-*m*-4-xylidine had b. p. 204·5—205°/747 mm. (Found: C, 80·3; H, 9·9%). *N*-Dimethyl-*m*-5-xylidine had b. p. 228·5—229°/772 mm. (Found: C, 80·8; H, 10·1%); picrate, m. p. 192° (Found: C, 50·9; H, 4·5. Calc. for $C_{16}H_{18}O_7N_4$: C, 50·8; H, 4·8%).

Reference has been made to the surprising similarity in b. p. of *N*-dimethyl- and *N*-acetylmethyl-xylidines. *N*-Acetomethyl-*m*-4-xylidide (Found: C, 74·5; H, 8·9. Calc. for $C_{11}H_{15}ON$: C, 74·6; H, 8·5%) boils at 205—205·5°/747 mm., only 0·5° higher than *N*-dimethyl-*m*-4-xylidine. The refractive indexes are also practically identical, but the densities differ considerably. Physical constants measured are as follows:

	$d_{4}^{14\cdot3°}$.	$d_{4}^{20\cdot6°}$.	$d_{4}^{21\cdot1°}$.	$d_{4}^{25°}$.	$n_{5461}^{25°}$.	$n_{5893}^{25°}$.	$n_{6563}^{25°}$.
N-Dimethyl-*m*-4-xylidine	0·92124	0·91621	—	0·91269	1·52230	1·51809	1·51325
N-Acetomethyl-*m*-4-xylidide	0·92672	—	0·92023	0·91696	1·52239	1·51817	1·51334

Molecular solution volumes in benzene solution.

	f_2.	$d_{4}^{25°}$.	M.S.V.	f_2.	$d_{4}^{25°}$.	M.S.V.
(Benzene)	—	0·87342	—	—	—	—
N-Dimethyl-*m*-5-xylidine	0·082768	0·88013	161·8	0·097186	0·88114	161·8
N-Dimethyl-*m*-4-xylidine	0·08647	0·87838	164·3	0·13041	0·88077	164·2
N-Dimethyl-*m*-2-xylidine	0·087024	0·87863	164·1	0·13002	0·88107	163·9

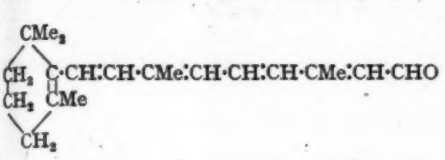
The author is indebted to Mr. James R. Sim and Mr. Victor C. Farmer for assistance with the experimental work, and to Mr. J. M. Cameron for the micro-analyses.

University of Glasgow. [*Received, March* 31*st*, 1944.]

NOTE.

Vitamin-A Aldehyde (Axerophthal). By E. G. E. Hawkins and R. F. Hunter.

Previous attempts to prepare vitamin-A aldehyde (axerophthal) by Oppenauer oxidation of vitamin-A alcohol in the presence of acetone (Batty, Burawoy, Harper, Heilbron, and Jones, J., 1938, 175) and diethyl ketone (Haworth, Heilbron, Jones, Morrison, and Polya, J., 1939, 128) led to the formation of axerophthylideneacetone and a C_{20} aldehyde whose ultra-violet absorption spectrum indicated that it contained a conjugated double bond more than vitamin-A aldehyde. The aldehyde has now been prepared by oxidation of vitamin-A alcohol with aluminium *iso*propoxide in the presence of acetaldehyde.



On Pondorff reduction, the aldehyde regenerated vitamin-A alcohol and on condensation with acetone in the presence of sodium ethoxide it furnished axerophthylideneacetone.

Ultra-violet spectroscopic measurements were made in purified *cyclo*hexane.

(i) A mixture of a distilled vitamin-A alcohol concentrate prepared from the unsaponifiable matter of whale liver oil ($E^{1\%}_{1\,cm.}$ = 1230 at 3250 A.) (1·2 g.), aluminium *iso*propoxide (2 g.), acetaldehyde (15 c.c.), and benzene (40 c.c.) was heated in a sealed tube at 70° for 48 hours. The product was treated with water and extracted with benzene, and the filtered extract dried with sodium sulphate and evaporated under reduced hydrogen pressure. The residue was dissolved in *cyclo*hexane (20 c.c.) and a portion of the solution was chromatographed on weakened "Mayfair" alumina under slight nitrogen pressure (cf. Hunter and Scott, *Biochem. J.*, 1941, **35**, 31). Elution of the main yellow zone furnished material which showed bands at 3680 and 3500 A., with a slight inflection at 3300 A. in the ultra-violet and maxima at 6580 and 6200 A. in the antimony trichloride reaction, indicating the presence of a small amount of unchanged vitamin-A alcohol. On treatment with alcoholic hydrogen chloride under the usual conditions (Hawkins and Hunter, *Biochem. J.*, 1944, **38**, 34) and further chromatography, however, a product was obtained which showed only a single band at 6570 A. in the antimony trichloride reaction. This material showed bands at 3650 and 3480 A. in the ultra-violet.

(ii) A further quantity of vitamin-A aldehyde was prepared in a similar manner from a chromatographed distilled concentrate of vitamin-A alcohol and was freed from unchanged vitamin-A alcohol by "cyclisation" and chromatography This showed bands at 3680 and 3500 A. in the ultra-violet ($E^{1\%}_{1\,cm.}$ = 1050 at 3680 A. and 920 at 3500 A.) and a maximum at 6570 A. ($E^{1\%}_{1\,cm.}$ = 2900) in the antimony trichloride reaction. The *dinitrophenylhydrazone*, prepared by heating with 2:4-dinitrophenylhydrazine in aqueous alcohol containing a small amount of hydrochloric acid in an atmosphere of hydrogen at 60° for 15 minutes, separated from acetone in brownish-black crystals, m. p. 208—209° (Found: C, 67·0, 66·9; H, 7·0, 7·1. $C_{36}H_{33}O_4N_4$ requires C, 67·25; H, 6·9%). This showed an absorption band at 4350 A. ($E^{1\%}_{1\,cm.}$ = 1060).

On Pondorff reduction with aluminium *iso*propoxide, vitamin-A aldehyde regenerated vitamin-A alcohol, which showed absorption maxima at 3300 A. and at 6200 A. in the ultra-violet and the antimony trichloride reaction respectively. This was characterised by conversion into "cyclised" vitamin-A, which showed absorption bands at 3900, 3700, and 3500 A. in the ultra-violet and a maximum at 6200 A. in the antimony trichloride reaction.

The aldehyde underwent fairly rapid oxidation on keeping in solution at 0°, yielding material which on chromatography on alumina furnished a main yellow zone containing a compound which showed a band at 3300 A. in the ultra-violet and at 6180—6200 A. in the antimony trichloride reaction. This differed from vitamin-A alcohol in that the ultra-violet absorption spectrum was unaltered after treatment with alcoholic hydrogen chloride in the usual way.

Synthesis of Axerophthylideneacetone from Vitamin-A Aldehyde.—A solution of vitamin-A aldehyde in acetone was cooled to −5°, treated with alcoholic sodium ethoxide, kept at laboratory temperature, with occasional shaking, for 2½ hours, and then extracted with benzene–light petroleum. The extract was washed in turn with dilute phosphoric acid, aqueous sodium carbonate, and water, and evaporated under reduced hydrogen pressure. The product showed main absorption bands at 3950 and 7320 A. in the ultra-violet and the antimony trichloride reaction respectively, characteristic of axerophthylideneacetone (Hawkins and Hunter, *loc. cit.*), which were not substantially altered by chromatography. On reduction with aluminium *iso*propoxide, the condensation product furnished axerophthylidene*iso*propyl alcohol which showed absorption bands at 3500 and 7130—7150 A, in the ultra-violet and the antimony trichloride reaction respectively (cf. Heilbron, Johnson, and Jones, J., 1939, 1563).

We thank the Directors of Lever Brothers and Unilever Ltd. for permission to publish these results.—Central Technical Department, Lever Brothers & Unilever Limited, Port Sunlight. [*Received, April 24th*, 1944.]

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111. *The Strengths of Six Monocarboxylic Acids in 25% Aqueous Acetone and 20% Aqueous Sucrose.*

By Idriswyn Davey and J. F. J. Dippy.

The dissociation constants of propionic, benzoic, phenylacetic, diphenylacetic, β-phenylpropionic, and cinnamic acids in 25% aqueous acetone and 20% aqueous sucrose at 25° have been measured by the conductivity method, and in both mixed solvents preserve the sequence observed in water (except K for diphenylacetic acid in aqueous acetone). It is significant, however, that the strengths in aqueous sucrose are consistently higher than those exhibited in water (diphenylacetic acid again excluded), despite the fact that the latter solvent has the greater dielectric constant. The behaviour of diphenylacetic acid in both solvents is distinctly anomalous.

The vast majority of dissociation constants of organic acids on record refer to aqueous solutions, and complete agreement has not been reached as to whether they will remain substantially in the same order if the solvent is changed. In a previous communication (Dippy, J., 1941, 550) the conclusion was reached, however, that the general sequence is interrupted in another solvent only by the incursion of special factors, and reference was made to the recent measurements of Elliott and Kilpatrick (*J. Physical Chem.*, 1941, **45**, 454, 466, 472) which showed that among several series of monosubstituted benzoic acids, examined in four different solvents, the truly anomalous members were salicylic, *o*-toluic, and *m*-hydroxybenzoic acids. In the first two of these

there is undoubtedly a " special factor " which is likely to be influenced by change of solvent (cf. Hammett, " Physical Organic Chemistry," McGraw Hill Book Co., 1940, p. 207). The sequence of strengths obtained in our measurements upon six monocarboxylic acids in 25% aqueous acetone and 20% aqueous sucrose have already been mentioned (Dippy, *loc. cit.*); it was our intention to extend the investigation, but as this is unavoidably postponed, we record the data thus far obtained. The actual values of 10^5K are included in Table I, together with the dissociation constants in water at the same temperature (*Chem. Reviews*, 1939, **25**, 151) for comparison.

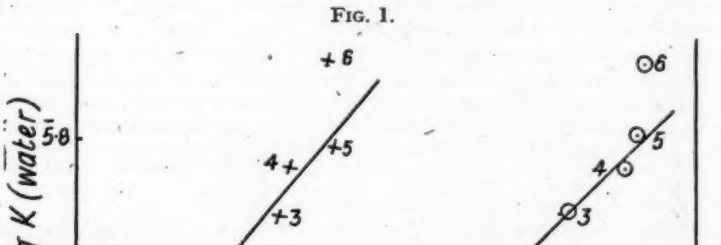
The values of dielectric constant (D) are due to Akerlöf (*J. Amer. Chem. Soc.*, 1932, **54**, 4125), and these are comparable with the figures quoted in International Critical Tables.

TABLE I.

Acid.	Dissociation constants (10^5K) at 25°. 25% Aqueous acetone ($D = 64{\cdot}0$).	20% Aqueous sucrose ($D = 73{\cdot}6$).	Water ($D = 78{\cdot}5$).
Diphenylacetic	0·653	7·43	11·5
Benzoic	0·681	6·55	6·27
Phenylacetic	0·499	5·53	4·88
Cinnamic (*trans*)	0·461	3·74	3·65
β-Phenylpropionic	0·240	2·23	2·19
Propionic	0·183	1·40	1·34

It will be seen that, if the result for diphenylacetic acid in aqueous acetone is omitted, the sequence of strengths of these acids in the two partly aqueous solutions is the same as for solutions in water. The most

FIG. 1.



Solvents: × 25% *Aqueous acetone.* ⊙ = 20% *Aqueous sucrose.*

Acids: 1 = *Propionic.* 2 = *β-Phenylpropionic.* 3 = *Cinnamic.* 4 = *Phenylacetic.* 5 = *Benzoic.* 6 = *Diphenylacetic.*

striking feature, however, is the fact that (diphenylacetic acid excluded) the strengths of the acids in 20% aqueous sucrose are distinctly *greater* than those for aqueous solution, despite the fact that the dielectric constant of the former is appreciably smaller than that of the latter solvent. This enhancement of strength recalls that observed by Bartlett and Dauber (*J. Amer. Chem. Soc.*, 1940, **62**, 1339) on addition of alcohols to a solution of hydrochloric acid in dioxan. A change of solvent means a change, not only in dielectric constant of the medium but also in chemical environment for the solute, and this alteration might make a marked contribution to the displacement of acid strengths; compared with acetone the molecule of sucrose must clearly exert a more influential chemical rôle. It is also noteworthy that Elliott and Kilpatrick (*loc. cit.*) have shown that certain organic acids exhibit different strengths in solvents of the same dielectric constant, and that Moore and Johns (*J. Amer. Chem. Soc.*, 1941, **63**, 3336) find that the K's of picric acid in certain ketones and nitriles are governed not so much by the dielectric constant of the medium as by the electron-sharing capacity of the radicals constituting it.

The strength of diphenylacetic acid is not so strikingly anomalous in aqueous acetone, but this is discerned by plotting log K_{water} against log K for the partly aqueous solvents in turn (a method of comparison used by La Mer, Kilpatrick, and others). Fig. 1 shows that, whereas a straight line connects the points representing five of the acids, that for diphenylacetic acid lies apart. If some spatial interaction of groups in the phenylacetic system has an effect upon acid strength, it can be expected (cf. Hammett, *op. cit.*) that the displacement of K with change of solvent will not follow the same trend as in acids in which the normal, recognised polar influences alone operate. This has been well illustrated by the data for the anomalous salicylic and *o*-toluic acids, and in view

of the similarity between *o*-toluic and phenylacetic acids, on spatial grounds, it seems reasonable to connect the abnormalities noted in both acids. The tendency in the phenylacetic system is favoured by the progressive substitution of phenyl groups, and does not become appreciable until diphenylacetic acid is reached. There is some evidence of slight abnormality in phenylacetic acid, however, if the data are examined along the lines employed by Wooten and Hammett (*J. Amer. Chem. Soc.*, 1935, **57**, 2289); both phenyl- and diphenyl-acetic acids show a diminution in relative strength when the acid is transferred from water to either partly aqueous solvent, and this is similar to the effect of transferring *o*-toluic acid, for example, from water to *n*-butyl alcohol as noted by these investigators. Although some form of spatial interaction has been implied as the cause of the anomalous behaviour of the phenylacetic acids, the present discussion is not concerned with the *nature* of the special effect operating; it needs only to be an effect which is modified differently by different solvents.

Experimental.

The conductivity measurements were made by means of the equipment and procedure described by Dippy and Williams (J., 1934, 161), but included in the bridge circuit was a variable condenser (max. capacity 0·002 μF.). The cells were of bottle type with blacked electrodes; two cells were used on each run. The "AnalaR" acetone was purified by the method of Dippy, Jenkins and Page (J., 1939, 1386). The aqueous acetone, containing 25% of acetone (w/v at 25°), was made from freshly distilled components for each individual run (κ = 0·65—1·2 gemmho). The 20% aqueous sucrose (w/v at 25°) was made from dried "AnalaR" sucrose (κ = 5·6—6·4 gemmho—this is a large increase upon the conductivity water, κ = *ca.* 1 gemmho).

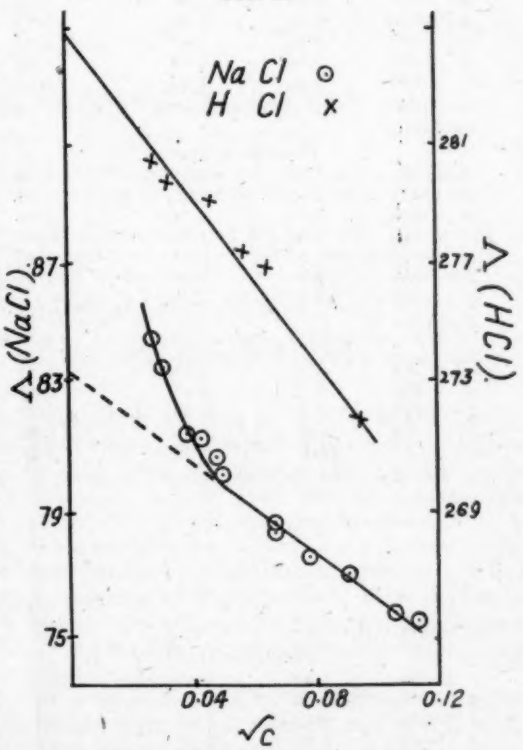
The organic acids were specimens prepared for earlier investigations, and the sodium salts were made as required (see Dippy and Williams, *loc. cit.*). The sodium chloride, of "AnalaR" quality, was recrystallised; the hydrochloric acid was also pure and redistilled (constant-boiling fraction).

Values of Λ_0 (acid) were obtained from series of measurements on solutions of the sodium salts, and the results were interpreted graphically with the use of the Debye–Hückel–Onsager equation as described in our earlier papers. To convert Λ_0 (salt) into Λ_0 (acid) the difference Λ_0 (HCl) − Λ_0(NaCl) ("normal" solvent corrected) had to be evaluated; for aqueous acetone this was 284·7 − 83·7 = 201·0. Whereas in the plot of Λ–$\sqrt{C}$ for hydrochloric acid all the points could be extrapolated, yet the solvent-corrected curve for sodium chloride was sensibly linear only between concentrations of 0·014 and 0·004 g.-mol./l. Both straight lines were inclined at approximately the angles of the theoretical Onsager slopes, *i.e.*, 53° and 35°, respectively (see Fig. 2). Unsatisfactory results were obtained with aqueous sucrose solutions of hydrogen chloride and sodium chloride. Hence, Λ_0(HCl) − Λ_0(NaCl) for this medium was derived by application of Walden's rule. When the rule is applied to sodium chloride in water and in 25% aqueous acetone the following agreement is noted:

	Λ_0.	η.	Product.
Water	126	0·008937	1·127
25% Aqueous acetone	84	0·01327	1·115

The value of 1·115 being used for the constant and that of 0·0171 for the viscosity of 20% aqueous sucrose, a figure of 156·3 is derived for Λ_0(HCl) − Λ_0(NaCl); the values of Λ_0 (acid) obtained by means of this are included in Tables IV and V. A regular fall in mobility occurs as the size of the anion increases, the sequence in both solvents being the same.

Fig. 2.



In calculating the dissociation constants of the acids, the normal solvent correction was applied to the measured conductivities; this is an arbitrary procedure. In simple aqueous solutions no solvent correction is applied in the case of weak acids, but with partly aqueous solutions the circumstances are quite different. In 25% aqueous acetone the acid possesses a strength one-tenth of that exhibited by it in water, and so Λ_0 is relatively small, yet the conductivity of the solvent has changed very slightly. Again, in the case of 20% aqueous sucrose the acid strengths compare with those in water but the conductivity of the solvent is considerably greater. Examination of the computations of K for a selected acid in each partially aqueous solvent (Table II) gives reasonable justification for the use of the "normal" solvent correction. Actually, it seems likely from our calculations that if the "true" solvent correction were known it would be rather less than the "normal" correction, and so in the case of aqueous sucrose solutions the enhancement of strength (compared with data for water) would be still further accentuated.

Table II.

	25% *Aqueous acetone.* β-Phenylpropionic acid.				20% *Aqueous sucrose.* Benzoic acid.		
10^3C.	$10^6K_{class.}$ (uncorr.).	$10^6K_{class.}$ (corr.).	$10^6K_{therm.}$ (corr.).	10^3C.	$10^5K_{class.}$ (uncorr.).	$10^5K_{class.}$ (corr.).	$10^5K_{therm.}$ (corr.).
9·786	2·62	2·48	2·41	5·023	7·71	6·93	6·61
4·466	2·67	2·47	2·41	2·051	7·93	6·63	6·39
2·587	2·64	(2·40)	(2·35)	1·811	8·35	6·91	6·67
1·518	2·75	2·45	2·41	1·163	8·76	6·84	6·63
1·225	2·76	2·42	2·38	0·674	9·14	6·41	6·25

The uncorrected classical dissociation constants rise steadily with increasing dilution and this trend is overcome by making the full solvent correction. Actually, the slight opposite trend noticeable in the corrected classical constants is to be anticipated, and this is more or less rectified when the thermodynamic constants are derived. The latter data were calculated along the orthodox lines (see Dippy and Williams, *loc. cit.*). The constants of the Onsager equation had to be deduced for these two media, as well as the values of A in the Debye–Hückel equation, $-\log f = A\sqrt{c_i}$. The following figures (based on bulk properties) were derived :

	a.	b.	A.
25% Aqueous acetone	0·3103	44·64	0·63
20% Aqueous sucrose	0·2516	32·58	0·54

TABLE III.

Cell constants : $a = 0{\cdot}1380$; $b = 0{\cdot}0734$.

25% Aqueous acetone solution.

10^3C (equiv./l.).	Λ.	$10^6K_{class.}$.	$10^6K_{therm.}$.	10^3C (equiv./l.).	Λ.	$10^6K_{class.}$.	$10^6K_{therm.}$.
Propionic acid.				Benzoic acid.			
a 13·54	3·10	1·93	1·87	*a* 14·09	5·73	7·01	6·71
a 7·586	4·09	1·90	1·85	*a* 6·877	8·30	7·28	7·02
a 5·014	5·00	1·87	1·83	*a* 4·819	10·0	(7·38)	(7·15)
b 4·087	5·54	1·88	1·84	*b* 3·662	11·2	7·08	6·87
b 2·471	7·09	1·88	1·84	*b* 2·355	13·8	7·06	6·87
b 1·746	8·35	1·84	1·81	*b* 1·496	17·4	7·17	7·01
$\kappa = 0{\cdot}80$ gemmho.	12 Determinations : Λ_0 (acid) = 261·0.			$\kappa = 0{\cdot}63$ gemmho.	11 Determinations : Λ_0 (acid) = 259·5.		
Phenylacetic acid.				Diphenylacetic acid.			
a 10·75	5·62	5·18	4·99	*a* 2·476	13·0	6·83	6·67
a 6·017	7·52	5·23	5·07	*a* 1·369	17·1	6·61	6·48
a 4·056	9·14	5·24	5·10	*a* 1·181	18·2	6·52	6·40
b 3·445	9·86	5·20	5·06	*b* 1·000	19·8	6·57	6·46
b 2·345	11·8	5·11	4·98	*b* 0·838	21·8	6·73	6·62
b 1·580	14·2	5·06	4·95	*b* 0·616	24·9	6·56	6·47
$\kappa = 0{\cdot}82$ gemmho.	16 Determinations : Λ_0 (acid) = 258·7.			$\kappa = 0{\cdot}80$ gemmho.	15 Determinations : Λ_0 (acid) = 254·5.		
β-Phenylpropionic acid.				Cinnamic acid.			
a 9·786	4·02	2·48	2·41	*a* 12·60	5·00	4·89	4·74
a 4·466	5·92	2·47	2·41	*a* 6·448	6·90	4·80	4·67
b 2·587	7·65	(2·40)	(2·35)	*a* 4·229	8·25	4·53	4·45
b 1·518	10·0	2·45	2·41	*b* 3·097	10·1	4·94	(4·85)
b 1·225	11·1	2·42	2·38	*b* 1·926	12·5	4·85	4·77
$\kappa = 0{\cdot}75$ gemmho.	10 Determinations : Λ_0 (acid) = 255·0.			$\kappa = 0{\cdot}91$ gemmho.	13 Determinations : Λ_0 (acid) = 255·6.		

TABLE IV.

Cell constants : $c = 0{\cdot}1411$; $d = 0{\cdot}0743$.

20% Aqueous sucrose solution.

10^3C (equiv./l.).	Λ.	$10^5K_{class.}$.	$10^5K_{therm.}$.	10^3C (equiv./l.).	Λ.	$10^5K_{class.}$.	$10^5K_{therm.}$.
Propionic acid.				Benzoic acid.			
c 21·68	5·41	1·47	1·40	*c* 5·023	23·0	6·93	6·61
c 10·30	7·63	1·41	1·36	*c* 2·051	34·1	6·63	5·39
c 9·128	8·23	1·46	1·40	*d* 1·181	36·7	6·91	6·67
d 7·508	8·86	1·40	1·35	*d* 1·163	44·5	6·84	6·63
d 6·267	9·64	1·38	1·34	*d* 0·6740	54·8	6·41	6·25
$\kappa = 6{\cdot}54$ gemmho.	21 Determinations : Λ_0 (acid) = 210·0.			$\kappa = 5{\cdot}89$ gemmho.	21 Determinations : Λ_0 (acid) = 207·2.		
Phenylacetic acid.				Diphenylacetic acid.*			
c 7·968	17·0	5·99	5·68	*c* 0·151	106·3	(8·92)	(8·74)
c 3·827	23·8	5·83	5·58	*c* 0·127	107·7	7·85	7·76
c 3·181	25·9	5·82	5·59	*d* 0·118	106·3	8·96	6·86
d 2·484	28·8	5·71	5·50	*d* 0·0947	115·5	7·33	7·24
d 1·097	42·4	5·91	5·73	*d* 0·0831	117·7	6·33	6·26
$\kappa = 6{\cdot}39$ gemmho.	15 Determinations : Λ_0 (acid) = 205·0.			$\kappa = 6{\cdot}29$ gemmho.	12 Determinations : Λ_0 (acid) = 201·2.		
β-Phenylpropionic acid.				Cinnamic acid.			
c 4·437	14·8	2·52	(2·43)	*c* 2·681	23·5	4·02	3·88
c 2·243	20·0	2·41	2·34	*c* 1·608	30·0	4·06	3·93
c 1·745	22·6	2·42	2·36	*c* 1·399	31·7	4·00	3·88
d 1·570	22·7	2·20	2·15	*d* 0·9980	35·8	3·71	3·61
d 1·246	25·5	2·24	2·18	*d* 0·8061	39·9	3·81	3·72
d 0·8140	31·4	2·29	2·23	*d* 0·6730	44·1	3·99	3·90
$\kappa = 5{\cdot}93$ gemmho.	16 Determinations : Λ_0 (acid) = 203·5.			$\kappa = 6{\cdot}10$ gemmho.	16 Determinations : Λ_0 (acid) = 204·3.		

* The small solubility of this acid in aqueous sucrose and the high conductivity of the solvent account for the less regular constants.

The results obtained with the six organic acids are contained in Tables III and IV (in each case the total number of determinations is indicated and one " run " is given in detail). The data for sodium chloride and hydrochloric acid in aqueous acetone are listed in Table V.

TABLE V.

Cell constants: $e = 0{\cdot}1380$; $f = 0{\cdot}0734$.

25% *Aqueous acetone.*

10^3C (equiv./l.).	$\sqrt{C}$.	$\Lambda_{corr.}$.	10^3C (equiv./l.).	$\sqrt{C}$.	$\Lambda_{corr.}$.	10^3C (equiv./l.).	$\sqrt{C}$.	$\Lambda_{corr.}$.
Hydrochloric acid.			Sodium chloride.					
e 9·486	0·097	271·6	*e* 11·36	0·107	75·77	*e* 13·36	0·116	75·36
e 4·055	0·064	276·9	*e* 6·395	0·080	77·50	*e* 8·519	0·092	76·91
f 3·022	0·055	277·2	*e* 4·541	0·068	78·56	*e* 4·471	0·067	78·48
f 1·995	0·045	278·8	*f* 2·531	0·050	80·61	*f* 2·738	0·052	79·86
f 1·112	0·033	279·5	*f* 1·585	0·040	81·35	*f* 1·873	0·043	81·10
f 0·7351	0·027	280·2	*f* 0·726	0·027	84·63	*f* 0·925	0·030	83·49
$\kappa = 1{\cdot}0$ gemmho.	Λ_0 (acid) = 284·7		$\kappa = 0{\cdot}70$ gemmho.	Λ_0 (acid) = 83·7		$\kappa = 0{\cdot}70$ gemmho.	Λ_0 (acid) = 83·7	

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112. *An Antibacterial Substance from* Aspergillus clavatus.

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An antibacterial substance from *Aspergillus clavatus* is identical with patulin from *Penicillium patulum*. Additional evidence for the chemical structure is presented which confirms the formulæ advanced by Raistrick *et al.* (*Lancet*, 1943, **245**, 625).

The isolation of β-*n*-propyl-γ-butyrolactone following reductive degradation and the isolation of γ-keto-β-methyl-*n*-hexoic acid, and the intermediates preceding its formation, *viz.*, αε-di-iodo-γ-keto-β-methyl-*n*-hexoic acid, 3-methyltetrahydro-γ-pyrone-2-carboxylic acid, and 3-chloromethylenetetrahydro-γ-pyrone-2-carboxylic acid, confirm the presence of a condensed system of two heterocyclic rings. Further experimental work helps to characterise the position and properties of the double bond and the keto-group. The results of oxidative and other degradations strongly suggest the existence of predominant tautomeric forms such as anhydro-4-hydroxy-5-hydroxymethyl-1 : 2-pyran-6-carboxylic acid and anhydro-4-hydroxy-5-hydroxymethyl-ene-5 : 6-dihydro-1 : 2-pyran-6-carboxylic acid.

AN antibacterial substance isolated from *Aspergillus clavatus* metabolism solution (cf. Bergel *et al.*, *Nature*, 1943, **152**, 750; Hooper *et al.*, *Science*, 1944, **99**, 16) has been shown by us to be identical with claviformin from *Penicillium claviforme* (Chain, Florey, and Jennings, *Brit. J. Exp. Path.*, 1942, **23**, 202) and very probably with patulin isolated from *Penicillium patulum*, Bainier, by Raistrick *et al.* (*Lancet*, 1943, **245**, 625). Through the courtesy of Professor Raistrick in furnishing a sample of patulin we were able to carry out mixed m. p.'s and thus conclusively established the identity of these three mould metabolites. Chain *et al.* (*Lancet*, 1944, **246**, 112) have shown independently the identity of patulin with claviformin by *X*-ray crystallographic examination. Many of our results on the degradation of this antibacterial substance are identical with those published for patulin; and in the following communication we wish to record only hitherto unpublished observations on the constitution of this chemically most interesting substance. In the absence of an accepted common name for this metabolite we have used the name clavatin as a convenient designation.

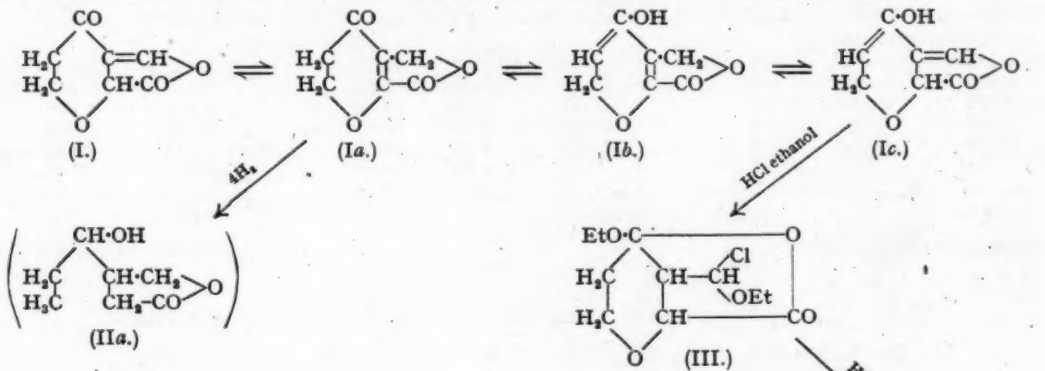
Raistrick *et al.* have based their proposed structure for patulin as anhydro-3-hydroxymethylenetetrahydro-γ-pyrone-2-carboxylic acid (I) mainly on the isolation, following acid hydrolysis, of formic acid and in 10% yield of tetrahydro-γ-pyrone-2-carboxylic acid; on the isolation of β-methylhexoic acid and β-methyl-γ-hexolactone, following hydrogenation and further reduction with hydriodic acid and red phosphorus; and on the formation in 60% yield of ε-iodo-γ-keto-*n*-hexoic acid by direct hydriodic acid treatment of patulin. In addition it was deduced from all the properties of patulin that the substituents in positions 2 and 3 of the pyrone ring are combined to an unsaturated lactone.

Similar evidence from alkaline titration and degradation of clavatin or derivatives led us early in our work to suspect the existence of an unsaturated lactone group. The identification of this group as an unsaturated butyrolactone and its relation to the remaining three carbon atoms of the molecule were established by the isolation of β-*n*-propylbutyrolactone (II*c*) from perhydrogenated clavatin after treatment with hydrobromic acid and reduction of the monobromide so obtained. The mechanism of the hydrogenation involved will be discussed later.

Our evidence for the structure of the remainder of the clavatin molecule, derived from ozonolysis, in which the main products were formic acid and glyoxal with traces of oxalic acid, did not enable us to envisage a simple oxygen ring system. The structure of a reduced γ-pyrone put forward by Raistrick *et al.* (*loc. cit.*) was based mainly on their isolation of tetrahydro-γ-pyrone-2-carboxylic acid. The low yield in which this substance was obtained, however, left room for further confirmatory evidence, which we now present. This is based on work in hand at the time of their publication.

Clavatin in ethanol solution on treatment with hydrogen chloride gave an oil, which was hydrolysed with dilute acid to a crystalline ketochloro-acid, $C_7H_9O_4Cl$. Hydrogenation of this substance gave as the main product a chlorine-free keto-acid, $C_7H_{10}O_4$, which on treatment with hydriodic acid was transformed into a

di-iodo-acid, $C_7H_{10}O_3I_2$. Replacement of the iodine atoms in this compound by hydrogen produced an acid, $C_7H_{12}O_3$, identified as γ-keto-β-methyl-*n*-hexoic acid (VII). The isolation of this compound and β-*n*-propylbutyrolactone (II*c*), as mentioned before, both containing all seven carbon atoms of clavatin, fixes definitely the relative positions of the keto-group and the original lactone group. The double bond in clavatin must therefore be in the αβ-position to the keto-group, a position suggested by the relationship between the ultraviolet absorption spectra of clavatin phenylhydrazone and dihydroclavatin phenylhydrazone.



Consideration of the structure and reactions of the intermediates preceding the formation of γ-keto-β-methyl-*n*-hexoic acid (VII) determined the nature and position of the fourth oxygen atom. The fact that the iodine of the di-iodo acid, $C_7H_{10}O_3I_2$, was easily removed with aqueous alkali to give a doubly unsaturated acid suggested that the iodine atoms were located in β- and β′-positions to the keto-group. The isolation of β-*n*-propylbutyrolactone being taken into consideration, this acid can only be formulated as *αε-di-iodo-γ-keto-β-methyl*-n-*hexoic acid* (VI). It follows that the parent substance, the monoketo-acid, $C_7H_{10}O_4$, must contain the fourth oxygen in cyclic ether linkage and is therefore *3-methyltetrahydro-γ-pyrone-2-carboxylic acid* (V).

An empirical formula $C_7H_7O_4Cl$ for the preceding chloro-acid was established by analysis and equivalent weight titrations. The presence of a keto-group was proved by hydroxylamine titration and the isolation of a dinitrophenylhydrazone. Addition of one mole of bromine and the uptake of two moles of hydrogen with elimination of chlorine established the presence of a double bond. The pattern of the alkaline titration, the preparation in high yield of ε-iodo-γ-keto-*n*-hexoic acid (IV*a*) by heating with hydriodic acid, and the simultaneous formation of formic acid and hydrogen chloride by alkaline degradation leave little doubt as to the existence of a chloromethylene group in the molecule. The substance is therefore *3-chloromethylenetetrahydro-γ-pyrone-2-carboxylic acid* (IV). It is noteworthy that, whereas the saturated pyronecarboxylic acid (V) gave on fission with hydriodic acid a di-iodo-compound (VI), the unsaturated acid (IV), as Raistrick *et al.* had found with patulin itself, underwent reduction at the 2-position during identical treatment and thus yielded a monoiodo-compound (IV*a*).

The precise constitution of the initial product obtained from clavatin by treatment with hydrogen chloride–ethanol is not so certain; but the following indications have been found. Analytical data indicated that it contained two ethoxy-groups and agreed approximately with the formula $C_{11}H_{17}O_5Cl$, and reactions showed that the substance was neutral and saturated. The isolation of two distinct 2 : 4-dinitrophenylhydrazones when the substance was treated with 2 : 4-dinitrophenylhydrazine in ethanol–sulphuric acid and in methanol–sulphuric acid respectively is explicable by assuming the acidolysis and alcoholysis of an etherified hydroxy-lactone, with accompanying loss of hydrogen chloride. These facts, together with the production of (IV*a*) by hydriodic acid degradation and the evidence as to position of the chlorine atom afforded by acid hydrolysis to (IV), can be reconciled in the formula (III).

With the existence of a *condensed system of two heterocyclic rings* firmly established, there remains to be discussed the position of the double bond and with it the peculiar character of the keto-group.

The acid and the alkaline degradations and the hydriodic acid treatment of clavatin and patulin (Raistrick *et al.*, *loc. cit.*) favour formula (I). However, the results of our hydrogenation experiments, together with the lack of optical activity and the behaviour of clavatin in the formation of its functional derivatives and in certain types of degradation, can only be explained by the coexistence of the tautomeric forms (I*a*, *b*, and *c*), to which Raistrick *et al.* have already alluded.

In contrast to the findings of Raistrick *et al.*, who report the addition of only 1 or 2 moles of hydrogen to patulin, the hydrogenation of clavatin under our conditions proceeded with the uptake of 3—4 moles of hydrogen. The complex nature of our product indicated that the reaction was not uni-directional and also that a considerable degree of polymerisation had taken place. The distillable material could be separated into neutral and acid fractions. The latter was not further investigated. The neutral fraction behaved as a lactone on titration. Treatment of a crude undistilled hydrogenation product with hydrobromic acid yielded a small amount of a lactone monobromide, $C_7H_{11}O_2Br$, which gave a crystalline *piperidino hydriodide*, $C_{12}H_{22}O_2NI$. The monobromide was hydrogenated to a bromine-free lactone, which yielded a phenylhydrazide identical with that prepared from β-*n*-propylbutyrolactone (II*c*). The bromo-lactone was not identical with α-bromo-β-*n*-propylbutyrolactone and, as it contained a $C{\cdot}CH_3$ group, the only remaining structure possible is that of β-(α′-*bromo*-n-*propyl*)*butyrolactone* (II*b*). The formation of the parent hydroxy-compound from clavatin may be explained by hydrogenolysis of the tautomeric form (I*a*) to give β-(γ′-hydroxy-α′-keto-*n*-propyl)butyrolactone, which was further hydrogenated to β-(α′-hydroxy-*n*-propyl)butyrolactone (II*a*), neither of which was isolated. We believe that the acidic fraction is formed by hydrogenolysis of the tautomeric form (I) (cf. Jacobs and Scott, *J. Biol. Chem.*, 1931, **93**, 139).

It was surprising to find that the keto-group in clavatin is acylated and etherified under unusually mild conditions, forming, *e.g.*, a monoacetate, *monobenzoate* and *monomethyl ether*. That these derivatives are hydrolysed with equal ease (cf. Raistrick *et al.*; *loc. cit.*) was shown by the close similarity of the hydroxylamine titration of clavatin and its acetate and by the formation of the same *oxime* from both these substances. Finally, clavatin could be regenerated from clavatin acetate by mild acid hydrolysis. Although it did not give any coloration with ferric chloride, we believe that under normal conditions the clavatin molecule exists predominantly in the enol forms (I*b*) and (I*c*). This was strongly supported by the almost identical ultra-violet absorption spectra of clavatin and its acetate, our inability to obtain a benzylidene derivative, and by the smooth formation of a considerable amount of glyoxal (at least 0·5 mol.) in the ozonolysis and permanganate oxidation of the mould metabolite. This involved the oxidative fission of the cyclic ether linkage (cf. Fischer, *Annalen*, 1929, **476**, 233). The small amount of oxalic acid and the large amount of formic acid (0·73 mol.) formed in these oxidations favour formula (I*c*) as the predominant tautomer.

Taking into consideration the smallness of the clavatin molecule, some of its reactions have been found unexpectedly complicated. This characteristic, as well as the very powerful effect which it exerts on biological systems, must be accepted as the functions of this unique chemical structure.

Experimental.

Isolation and Purification of Clavatin.—The crude concentrate of clavatin (Wiesner, *Nature*, 1942, **149**, 357) was further purified by treatment with a small amount of warm water, which dissolved all the clavatin and left a residue of phenolic by-product. Concentration of the aqueous solution gave an oil in early experiments; later it was always obtained crystalline. From the non-crystalline concentrate, crystalline derivatives such as the acetate (m. p. 118—120° *ex* methanol) and phenylhydrazone (m. p. 149—150°) were readily obtained. Pure clavatin was obtained from the crystalline concentrate by pressing it on porous plate and crystallising the oil-free material several times from chloroform (charcoal); m. p. 109·5—110·5° (Found: C, 54·2; H, 3·8. Calc. for $C_7H_6O_4$: C, 54·5; H, 3·9%).

Molecular-weight determinations were carried out on clavatin and its acetate by the cryoscopic method. The value indicated for clavatin in acetic acid solution was 172 ± 5, and in nitrobenzene solution, 150 ± 4. The value found for clavatin acetate in acetic acid solution was 198 ± 5.

The phenolic by-product, crystallised from methanol–water, had m. p. 184—186° and empirical formula $C_{10}H_{12}O_3$. It did not possess any antibacterial activity. Work on its constitution will be reported later.

Some Properties of Clavatin and Clavatin Acetate.—The ultra-violet absorption spectrum of clavatin consists of a single band having $\lambda_{max.}$ at 2765 A., $\varepsilon_{max.}$ 16,600. That of clavatin acetate is very similar, the single band having a maximum at 2770 A., $\varepsilon_{max.}$ 17,600.

Treatment of clavatin or the acetate with bromine in glacial acetic acid resulted in the slow absorption of one molecular equivalent. The products were viscous liquids which could not be induced to crystallise. In chloroform solution clavatin and the acetate did not react with bromine or with perbenzoic acid.

An alkaline hydrolysis of clavatin, performed in a closed system, gave a distillate which yielded a trace of crystalline 2 : 4-dinitrophenylhydrazone, m. p. 120—122° after recrystallisation. A mixed m. p. with acetone-2 : 4-dinitrophenylhydrazone was not depressed; but a large depression resulted from admixture with the 2 : 4-dinitrophenylhydrazone of methyl ethyl ketone.

A hydroxylamine titration was performed in the following manner: Aqueous solutions were prepared: (A) of clavatin (0·33 mM in 5 ml.), (B) of hydroxylamine hydrochloride (2 mM in 5 ml.), (C) of sodium hydroxide (1 mM in 5 ml.). A number of mixtures containing 5 ml. each of (A), (B) and (C) were prepared, kept at room temperature for definite periods, and then titrated to the end-point of bromophenol-blue with N/10-hydrochloric acid. Typical runs were as follows: after ½ hour, 6·63 ml.; after 1 hour, 5·24 ml.; and after 3½ hours, 3·2 ml. Titration of a mixture containing (B) (5 ml.) and (C) (5 ml.) required 10·0 ml. of acid. The results indicate absorption of 1 molar equivalent of hydroxylamine in ½—1 hour and of 1·9 molar equivalents within 3½ hours. A yellow colour developed in the solutions soon after mixing and gradually increased in depth, so that it was impossible to observe the indicator colour change in runs of more than 3½ hours' duration.

An experiment carried out in the same manner with clavatin acetate gave very similar results as regards amount and rapidity of hydroxylamine uptake. There was also a development of yellow colour and appreciable buffering at the end-point due to liberated acetic acid.

Clavatin acetate (0·5 g.), shaken with 0·2N-hydrochloric acid (5 ml.), gradually passed into solution. After neutralisation this solution was evaporated to dryness to give an oily residue. A chloroform extract deposited crystals which were identified as clavatin.

Other Derivatives of Clavatin.—*Clavatin oxime* (as I or I*a*). From a solution of clavatin (0·5 g.) and hydroxylamine hydrochloride (0·55 g.) in 0·2N-hydrochloric acid (5 ml.) at 20°, *clavatin oxime* slowly crystallised during about 3 days. Recrystallised from water, it had m. p. 152—153° (decomp.) (Found: C, 49·6; H, 4·3; N, 8·3. $C_7H_7O_4N$ requires C, 49·6; H, 4·2; N, 8·3%). This oxime was also formed when clavatin acetate was shaken with a solution of hydroxylamine hydrochloride in 0·2N-hydrochloric acid.

Clavatin oxime monoacetate. Acetylation of clavatin oxime with acetic anhydride and pyridine in the usual manner yielded a *monoacetate* which, recrystallised from dilute acetic acid, had m. p. 82—84° (Found: C, 51·2; H, 4·7; N, 5·8. $C_9H_9O_5N$ requires C, 51·2; H, 4·3; N, 6·6%).

Dihydroclavatin phenylhydrazone. The red solution of clavatin phenylhydrazone (2·4 g.) in ethanol (250 ml.) was shaken with hydrogen in presence of a neutral catalyst prepared from charcoal (1 g.) and 5% palladous chloride solution (6 ml.) until approximately one molar equivalent of hydrogen had been absorbed. The alcoholic solution, which was now yellow, was filtered from catalyst and concentrated to dryness at 12 mm. The crystalline product, recrystallised from methanol, had m. p. 180—183° and was shown to be identical with the phenylhydrazone prepared from crude dihydroclavatin (Raistrick *et al.*, *loc. cit.*) by the action of phenylhydrazine hydrochloride (Found: C, 63·2; H, 5·5; N, 11·7. Calc. for $C_{18}H_{14}O_3N_2$: C, 63·4; H, 5·7; N, 11·4%).

The ultra-violet absorption spectrum of this compound has maxima at 3800 A. and at 2490 A.; $\varepsilon_{max.}$ respectively 35,700 and 15,400. This shows a general shift towards shorter wave-lengths as compared with the ultra-violet absorption spectrum of clavatin phenylhydrazone, which has $\lambda_{max.}$ 4130 A. and 2690 A.; $\varepsilon_{max.}$ respectively 17,400 and 13,300.

Clavatin methyl ether (as I*b* or I*c*). Clavatin (1·0 g.), dissolved in anhydrous ether (10 ml.) and methyl iodide (4 ml.), was refluxed with dry silver oxide (2·3 g.) for 40 hours. The liquid was filtered, and the residue washed with ether. Evaporation of solvent left a pale yellow oil which crystallised completely. The compound was unstable and could not be recrystallised from solvent, but it sublimed readily at 45—50°/0·1 mm. in colourless stars, m. p. 69—71° (Found: C, 57·2; H, 5·1; OMe, 17·2. $C_8H_8O_4$ requires C, 57·1; H, 4·8; OMe, 18·4%). On standing at room temperature even in a sealed tube, a fall in m. p. was apparent within 12 hours, and the whole material was rapidly transformed into an unsublimable, non-melting polymer.

Clavatin benzoate (as I*b* or I*c*). Clavatin (0·31 g.) was treated with benzoic anhydride in pyridine, and the product worked up in the usual manner. The crystalline substance (0·36 g.) obtained, recrystallised from methanol, formed colourless needles, m. p. 143·5—144·5° (Found: C, 64·8; H, 4·0. $C_{14}H_{10}O_5$ requires C, 65·1; H, 3·9%).

Hydrogenation of Clavatin.—Hydrogenation in 90% ethanol–water or acetic acid at normal pressure with a palladium–charcoal catalyst resulted in hydrogen uptakes varying from 2·9 to 4·0 molar equivalents and produced oils containing *ca.* 90% of lactone and 10% of acid. The crude products reacted with phenylhydrazine or hydrazine hydrate in ethanol; but crystalline derivatives did not result. The hydrogenation products resinified on heating and only small heterogeneous distillates could be obtained. One such distillate (1·0 g.), b. p. 143—149°/15 mm., gave with phenylhydrazine a crystalline substance, which was recrystallised from ethyl acetate and finally from ethanol–water, forming nearly colourless plates, m. p. 164—166° (Found: C, 67·1; H, 7·0; N, 16·5; *C*-Me, 0·6. $C_{19}H_{24}O_2N_4$ requires C, 67·0; H, 7·0; N, 16·5%). Negative Knorr tests were obtained on this substance and on the product of treatment with sodium in ethanol.

In a pressure hydrogenation, clavatin (3·0 g.), Adams's catalyst (0·3 g.), and glacial acetic acid (170 ml.) were stirred at room temperature for 45 minutes under a hydrogen pressure of 110 atms. A second portion of catalyst (0·2 g.) was added, and the mixture stirred for a further 3 hours. The catalyst was filtered off, and the solvent evaporated under 15 mm. The product, dissolved in 49% hydrobromic acid (50 ml.), was heated in a bomb tube at 110—120° for 4 hours. The cooled reaction mixture, containing some charred material, was diluted with water (50 ml.) and extracted four times with ether (50 ml. portions). The combined ethereal extracts were washed twice with water, twice with ice-cold N-sodium carbonate, again with water, and finally dried over sodium sulphate. Evaporation of the ether left a greyish-yellow oil (1·68 g.). On distillation this material (1·4 g.) yielded a pale yellow oil (0·75 g.), b. p. 175—180°/15 mm. [Found: C, 40·5; H, 5·3; Br, 41·8. $C_7H_{11}O_3Br$ (II*b*) requires C, 40·6; H, 5·3; Br, 38·8%].

Hydrogenation of the *monobromide* (0·7 g.), dissolved in ethanol (70 ml.) and water (10 ml.), with a palladium–charcoal catalyst (1·0 g.) yielded an oil (0·39 g.), for which alkaline titration indicated a lactone : acid ratio of 7 : 1 and an equivalent weight of 145. This crude hydrogenation product (0·37 g.) was dissolved in ethanol (5 ml.) containing phenylhydrazine (0·32 g.), and the mixture refluxed for 3 hours. The solvent was evaporated, and the residual oil leached with dry ether. A small amount of ether-insoluble solid was found to be phenylhydrazine hydrobromide. The ethereal solution yielded on evaporation an oil which crystallised almost completely. Treatment with benzene separated this material into colourless crystals and a red oil, from which more crystalline material was obtained after a further reaction with phenylhydrazine (0·1 g.). Combined crystals (0·12 g.) from these procedures were recrystallised from benzene, separating in small lustrous plates, m. p. 112·5—113·5° [Found: C, 66·0; H, 8·7; N, 12·1. Calc. for $C_{13}H_{20}O_2N_2$ (cf. II*c*): C, 66·1; H, 8·5; N, 11·9%]. A mixed m. p. with the phenylhydrazide from β-propylbutyrolactone prepared according to Clutterbuck *et al.* (*Biochem. J.*, 1937, **31**, 987) was not depressed.

Perhydroclavatin monobromide (0·25 g.) obtained in a second experiment was dissolved in benzene (3 ml.), and freshly distilled piperidine (0·23 ml.) added. On 3 days' standing at room temperature, long colourless needles separated and were identified as piperidine hydrobromide (0·15 g.). Benzene was evaporated from the filtrate, and the residue leached with dry ether. A small amount of gummy insoluble material was removed, and the ethereal solution extracted twice with 2N-hydrochloric acid (10 ml.). The acid aqueous phase was cooled to 0° and made alkaline by slow addition of ice-cold 2N-sodium hydroxide (22 ml.). Two extractions with ether then removed from the alkaline mixture a viscous, almost colourless oil (0·17 g.). This substance was dissolved in freshly distilled acetone (25 ml.), and N-alcoholic hydrogen chloride (0·8 ml.) added. After a few minutes, sodium iodide (0·2 g.) in acetone (10 ml.) was added, and the mixture kept for 30 minutes with occasional agitation. Precipitated sodium chloride was filtered off, and the hydriodide recovered as an oil by evaporation of the acetone. It became crystalline on addition of ethyl acetate and was recrystallised from ethanol (2·5 ml.) and ethyl acetate (6 ml.); m. p. 170—171° (Found: C, 42·3; H, 6·4; N, 4·6; I, 35·3; *C*-CH_3, 3·6. $C_{12}H_{22}O_2NI$ requires C, 42·5; H, 6·5; N, 4·1; I, 37·5; *C*-CH_3, 7·1%).

Hydrogenation of Clavatin Acetate.—Clavatin acetate (0·5 g.) in ethanol (50 ml.) was added to a neutral washed catalyst prepared from Merck charcoal (1·0 g.) and palladous chloride (0·15 g.) suspended in water (50 ml.); 3·65 molar equivalents of hydrogen were absorbed in 1¼ hours. Catalyst was filtered off and washed with water. The combined filtrate and washings were evaporated until distillation at 15 mm. ceased with a bath temperature of 50°. The distillate contained acid equivalent to 26·1 ml. of N/10-alkali, which was isolated as a *S*-benzylthiuronium salt, m. p. 143—144°. A mixed m. p. with *S*-benzylthiuronium acetate was undepressed.

In a repetition of the above experiment with nitrogen replacing hydrogen, the liquid was filtered and distilled after 2½ hours' shaking with the catalyst. The distillate contained 91% of the theoretical quantity of acetic acid. The distilland and residue did not crystallise on seeding with clavatin and had physical properties suggestive of polymerisation.

Ozonolysis of Clavatin.—A solution of clavatin (1·0 g.) in water (50 ml.), cooled to 0—5°, was treated with ozonised oxygen for 3½ hours. The ozonised solution was kept for 20 hours at room temperature and then evaporated in a vacuum until distillation ceased with a bath temperature maximum of 40°. Distillate—Fr. 1; distilland—Fr. 2.

Fr. 1 gave a positive test with Schiff's reagent and required the addition of 47·6 ml. of 0·1N-sodium hydroxide (0·73 molar equivalent) for neutralisation to pH 6·5. The neutralised solution was evaporated, and the distillate (Fr. 3) collected. The residue of sodium salt was converted into a *S*-benzylthiuronium salt, and the latter recrystallised from methyl ethyl ketone. It formed laminæ, m. p. 150—151° (Found: C, 50·1; H, 5·6; N, 12·9; S, 14·9. Calc. for $C_9H_{12}O_2N_2S$: C, 50·9; H, 5·7; N, 13·2; S, 15·1%), identified by mixed m. p. as *S*-benzylthiuronium formate.

Fr. 3 with Brady's reagent gave an orange-yellow, apparently amorphous powder (0·27 g.), m. p. 322—324° (frothing). Two crystallisations from nitrobenzene gave dark red needles, m. p. 334—335° (frothing) (Found: C, 40·4; H, 2·5; N, 26·5. Calc. for $C_{14}H_{10}O_8N_8$: C, 40·2; H, 2·4; N, 26·8%). A mixed m. p. with the bis-2 : 4-dinitrophenylhydrazone of glyoxal was undepressed.

Fr. 2, a medium yellow, viscous oil (1·09 g.), was taken up in water (50 ml.), the solution acidified to Congo-red and refluxed for 30 minutes. It was then treated with a slight excess of 2 : 4-dinitrophenylhydrazine in ethanol and heated. The solid was filtered off (Filtrate—Fr. 4), washed, and dried (1·1 g.), m. p. 315—320° (frothing). A portion was triturated with cold 15% sodium carbonate solution (10 ml.); but very little colour appeared in solution and only a trace of amorphous solid was deposited when the filtrate was acidified. The fraction insoluble in sodium carbonate crystallised readily from nitrobenzene and the purified material was identified as the bis-2 : 4-dinitrophenylhydrazone of glyoxal (total amount isolated, 0·5 molar equivalent).

Fr. 4 was evaporated, the residue treated with water (100 ml.), and the extract decolourised with charcoal. Evaporation of the solution gave a crystalline solid (0·27 g.), which in aqueous solution required 38·6 ml. of 0·1N-sodium hydroxide for neutralisation to pH 6·5. The resultant sodium salt was extracted with hot ethanol, a small amount of oil, which was not further examined, thereby being removed. The ethanol-insoluble fraction, treated with *S*-benzylthiuronium chloride, yielded a gummy solid (0·28 g.) which slowly crystallised. It was extracted first with boiling methyl ethyl ketone and then with boiling ethanol. The insoluble residue crystallised from water in small plates, m. p. 199—200° (frothing). A mixed m. p. with *S*-benzylthiuronium oxalate was undepressed. The ethanol extract contained a solid (0·15 g.) which crystallised from ethanol (12 ml.) in long colourless needles, m. p. 154·5—155·5° (frothing) (Found: C, 50·4; H, 5·4; N, 12·5; S, 13·5. $C_{20}H_{24}O_8N_4S_2$ requires C, 51·7; H, 5·2; N, 12·1; S, 13·8. $C_{19}H_{22}O_4N_4S_2$ requires C, 50·7; H, 4·9; N, 12·5; S, 14·2%). A mixed m. p. with *S*-benzylthiuronium *dl*-malate [m. p. 152—153·5° (slow frothing)] was depressed. *S*-Benzylthiuronium ketosuccinate (from hydroxyfumaric and hydroxymaleic acids), m. p. 125—126° (frothing), and *S*-benzylthiuronium ethylene oxide dicarboxylate, m. p. 184—186° (frothing), were prepared in unsuccessful attempts to identify this compound.

A second ozonolysis of clavatin in chloroform solution gave qualitatively identical results.

Oxidation of Clavatin by Permanganate.—To a stirred solution of clavatin (0·5 g.) in water (20 ml.), cooled in ice, was added dropwise a solution of potassium permanganate (1·37 g.) in water (150 ml.) during 5 hours, decolorisation of the entering salt being instantaneous during the whole period. The filtrate from manganese dioxide was acidified and worked up substantially as described for the ozonolysis. 0·92 Molar equivalent of distillable acid was identified as formic acid and a small amount of glyoxal obtained in the form of its bis-2 : 4-dinitrophenylhydrazone. Addition of Brady's reagent to the distilland produced an orange-red flocculent precipitate (0·5 g.), having an indefinite decomposition m. p. *ca.* 160°. It was not found possible to crystallise this substance and it was not further examined.

Treatment of Clavatin with Hydrogen Chloride in Ethanol.—Dry hydrogen chloride was passed into a solution of clavatin (4·4 g.) in ethanol (70 ml.) cooled to −10°. Saturation of the solution was complete in 6 hours. Benzene (50 ml.) was added to the reaction product, and the mixture evapotated under a water pump vacuum to a small volume. After a second addition of benzene and subsequent evaporation, the residual solution was diluted with benzene (150 ml.) and transferred to a separating funnel. This solution was then washed once with water (20 ml.), twice with 1% sodium bicarbonate solution (30 ml. portions), twice with water (20 ml.), and finally dried over sodium sulphate. Removal of solvent left a pale yellow-brown oil (5·9 g.). A portion kept at room temperature showed progressive development of amorphous ethanol-insoluble substance and underwent gradual resinification. The *substance* distilled, with a very small forerun, at 114—116°/0·15 mm. as a colourless oil (4·4 g.) (Found: C, 50·5; H, 5·6; Cl, 13·6; OEt, 26·8. $C_{11}H_{17}O_6Cl$ requires C, 49·9; H, 6·4; Cl, 13·4; OEt, 34·0%). Gradual decomposition took place in the distilland, producing a dark brown resin.

Reactions and Derivatives of Substance $C_{11}H_{17}O_6Cl$ (III).—Quantitative studies with freshly distilled material showed that (*a*) bromine was not absorbed from acetic acid or chloroform solution; (*b*) no reaction occurred with monoperphthalic acid in ethereal solution.

2 : 4-*Dinitrophenylhydrazones.* Freshly prepared crude material (0·53 g.), dissolved in ethanol (5 ml.), was added to a solution of 2 : 4-dinitrophenylhydrazine (0·2 g.) in sulphuric acid (0·4 ml.) and ethanol (3 ml.). A red colour rapidly developed and orange-coloured crystals separated. Recrystallised three times from benzene (3 ml.) and light petroleum (b. p. 40—60°) (6 ml.), the substance had m. p. 168—170° (frothing) (Found: C, 49·4; H, 4·9; N, 13·8; Cl, 1·8; OEt, 20·2. $C_{17}H_{23}O_8N_4$ requires C, 50·0; H, 5·1; N, 13·7; OEt, 22·2. 23% $C_{17}H_{21}O_8N_4Cl$ +77% $C_{17}H_{20}O_8N_4$ require C, 49·0; H, 4·8; N, 13·5; Cl, 1·8; OEt, 21·6%).

The experiment was repeated, methanol being used in place of ethanol. Crystals, similarly recrystallised, had m. p. 164—166° (frothing), depressed on admixture with the substance, m. p. 168—170°, from ethanol solution (Found: C, 48·0; H, 4·5; N, 13·7; Cl, 1·5. $C_{16}H_{18}O_8N_4$ requires C, 48·6; H, 4·6; N, 14·1. 18·2% $C_{16}H_{19}O_8N_4Cl$ +81·8% $C_{16}H_{18}O_8N_4$ require C, 47·9; H, 4·5; N, 14·0; Cl, 1·5%).

Degradation by hydriodic acid. Freshly prepared crude material (0·4 g.), dissolved in hydriodic acid (*d* 1·7) (13 ml.), was heated in an atmosphere of carbon dioxide for 2 hours, the bath temperature being raised gradually from 70° to 125° during 1 hour and then maintained at 130—135° for 1 hour. The reaction mixture was cooled, diluted with water (30 ml.) and extracted with ether (200 ml.) in four portions. The combined ethereal extracts were washed with water (20 ml.), in two portions, with small volumes of N-sodium thiosulphate until colourless, finally with water (40 ml.) in three portions, and dried over sodium sulphate. Removal of solvent yielded an oil (0·35 g.) which crystallised immediately. Recrystallised from benzene, it melted at 92—94°. A mixed m. p. with ε-iodo-γ-ketohexoic acid (IV*a*) was not depressed.

Acid hydrolysis. Freshly prepared crude reaction product (5·9 g.) obtained in a second experiment was dissolved in ethanol (50 ml.) and 2N-sulphuric acid (70 ml.), and the solution boiled in a nitrogen atmosphere so that slow distillation took place. Boiling was continued in this manner for 2 hours, additions of water being made when the volume reached one-third of the original. At the end of the period, the solution was evaporated under 15 mm. pressure until distillation ceased. The distilland residue crystallised during this procedure. The distillate required 31·8 ml. of N/10-sodium hydroxide for neutralisation to pH 6·5.

Analysis showed that 49% of the distillate acid was hydrochloric, and 51% formic acid.

The crystalline distilland residue was filtered off, washed with ice-cold 2N-sulphuric acid (15 ml.) in four portions, with ice-cold water (20 ml.) in five portions, and finally dried in a vacuum over phosphoric oxide. The product was a light brown, crystalline solid (2·75 g.), m. p. 128·5—129·5°. A further quantity (0·3 g.) was obtained by working up the mother-liquors. The total yield was dissolved in chloroform (100 ml.), the boiling solution treated with charcoal and evaporated to *ca.* 30 ml. On cooling, colourless needles separated (2·58 g.), m. p. 129—130° [Found: C, 43·8; H, 3·8; Cl, 18·4. $C_7H_7O_4Cl$ (IV) requires C, 44·1; H, 3·7; Cl, 18·6%].

Reactions and Derivatives of the Chloro-acid (IV).—*Titrations.* An aqueous solution was acid to Congo-red but gave no coloration with ferric chloride. Titration of the acid group with N/50-sodium hydroxide to pH 4·9 indicated an equivalent weight of 197 and titration to pH 6·5, one of 185. Slow further absorption of alkali beyond the first transient indicator colour occurred at room temperature to a total of 3 molar equivalents (assuming *M*, 190·5). A typical experiment is described in detail.

To the chloro-acid (IV) (0·0828 g.) in water (5 ml.), N/10-sodium hydroxide was added, phenolphthalein being used as an indicator. The first indicator colour, lasting 5 secs., was obtained with 4·58 ml. A further 9·16 ml. of alkali were added dropwise during 24 hours, the mixture being stored at −15° overnight. Speed of indicator colour discharge slowed progressively during entry of the third molar equivalent. The final indicator colour was stable for 30 minutes. The solution contained as ionised chlorine 82% of the chlorine content of the starting material.

A strongly alkaline solution of the chloro-acid was boiled for 15 minutes. The mixture was acidified and distilled. In the distillate formic and hydrochloric acids were identified by methods previously described. Oxalic acid could not be detected in the distilland.

Degradation by hydriodic acid. The chloro-acid (0·198 g.) was dissolved in freshly distilled hydriodic acid (*d* 1·7) (10 ml.), and the solution treated and finally worked up as described previously. Removal of solvent left an oil (0·24 g.) which crystallised rapidly and completely. Crystallisation from benzene gave a substance, m. p. 92—94°. A mixed m. p. with ε-iodo-γ-ketohexoic acid (IV*a*) was undepressed.

Hydroxylamine titration. This was carried out substantially as described for clavatin, chloro-acid (0·1 mM), hydroxylamine hydrochloride (0·56 mM), and sodium hydroxide (0·38 mM) being used for each determination. The solutions were titrated to pH 4·8, a lower pH being impossible owing to buffering caused by the carboxyl group of the chloro-acid. At pH 4·8 only about 82% of the free hydroxylamine was titrated. Titrations indicated that in 1½ hours 0·80, in 3 hours 0·82, and in 18 hours 0·84 molar equivalent of hydroxylamine was absorbed.

2 : 4-*Dinitrophenylhydrazone.* The chloro-acid (IV) (0·2 g.) in ethanol (2 ml.) was added to a solution containing 2 : 4-dinitrophenylhydrazine (0·15 g.) in sulphuric acid (0·3 ml.) and ethanol (2·2 ml.). An orange-coloured solid was deposited and was filtered off after 2 days (0·10 g.). In two crystallisations from benzene it separated in rosettes of red needles, m. p. 189—190° (Found: C, 45·9; H, 3·8; N, 14·6; Cl, 9·0; OEt, 10·4. $C_{15}H_{15}O_7N_4Cl$ requires C, 45·2; H, 3·8; N, 14·1; Cl, 8·9; OEt, 11·3%). The substance did not dissolve in sodium carbonate solution and the Knorr pyrazoline test was negative. Esterification of the carboxyl group had apparently taken place.

Bromine addition. The chloro-acid (IV) (0·0934 g.) in glacial acetic acid (5 ml.) was treated with bromine (0·16 g.), and the residual bromine estimated by the usual method. The bromination required 11·25 ml. of 0·1N-sodium thiosulphate as compared with 18·8 ml. for the control. Further iodine was rapidly liberated on standing after the first end-point had been reached.

In a second experiment, the chloro-acid (IV) (0·0927 g.) in chloroform (5 ml.) was mixed with bromine (0·16 g.) in chloroform (1 ml.). There was a rapid reduction in colour as compared with a control solution. After standing overnight, the solvent was evaporated under 0·1 mm. The solvent-free residue was a viscous oil (0·17 g.). This substance was dissolved in ethanol (10 ml.) and titrated with N/20-sodium hydroxide: 11·4 ml. were required to bring the pH to 6·5 and on standing further acid rapidly appeared. In 36 hours a further total of 11·06 ml. of N/20-sodium hydroxide were required for neutralisation. The final end-point was stable.

Hydrogenation. Neutral washed catalyst prepared from Merck charcoal (0·15 g.) and 10% palladous chloride solution (0·25 ml.) was suspended in water (20 ml.) under hydrogen. The chloro-acid (IV) (1·48 g.), dissolved in water (30 ml.), was added. During 1 hour a total of 2·4 molar equivalents of hydrogen were absorbed. Catalyst was filtered off, and the colourless filtrate evaporated under 15 mm. to a viscous oil (1·23 g.). A portion of this material (0·014 g.), dissolved in water and titrated with N/20-sodium hydroxide, required 3·95 ml. for neutralisation to pH 6·5. On boiling, neutralisation of a further 0·4 ml. occurred slowly. The remaining material was dissolved in water, and the cold solution brought to pH 6·5 by cautious addition of sodium hydroxide and extracted continuously with ether for 7 hours. The extracted solution was evaporated to dryness, the residue dissolved in water (3 ml.) and ethanol (17 ml.), and this solution divided into four equal parts.

From three parts the following derivatives were prepared by methods in general use: S-*Benzylthiuronium* salt, crystallised from methyl ethyl ketone, m. p. 149—150° [Found: C, 56·0; H, 6·4; N, 8·6; S, 9·6. $C_{15}H_{20}O_4N_2S$ (cf. V) requires C, 55·6; H, 6·2; N, 8·6; S, 9·9%]; p-*phenylphenacyl* ester, crystallised four times from benzene–light petroleum (b. p. 60—80°) and twice from ethanol, burrs of colourless needles, m. p. 125—127° [Found: C, 71·2; H, 5·9; *C*-CH_3, 1·6. $C_{31}H_{30}O_5$ (cf. V) requires C, 71·6; H, 5·7; *C*-CH_3, 4·3%]; 2 : 4-*dinitrophenylhydrazone*, crystallised twice from 80% ethanol–water and twice from toluene, m. p. 197—199° [Found: C, 46·3; H, 4·1; N, 16·2. $C_{13}H_{14}O_7N_4$ (cf. V) requires C, 46·2; H, 4·1; N, 16·6%].

Isolation of γ-Keto-β-methylhexoic acid (VII). The fourth portion was evaporated to dryness, and the residue dissolved in freshly distilled hydriodic acid (*d* 1·7) (12 ml.). This solution was treated and worked up as previously described for hydriodic acid degradations. In this way there was obtained a pale yellow oil which crystallised completely (0·45 g.). A portion for analysis was crystallised twice from light petroleum (b. p. 100—120°) after treatment with charcoal, separating in feathery aggregates of needles, m. p. 103—105° [Found: C, 21·4; H, 2·6; I, 62·3. $C_7H_{10}O_3I_2$ (VI) requires C, 21·2; H, 2·5; I, 64·1%].

The substance (0·0252 g.), dissolved in ethanol (3 ml.) and water (2 ml.) and titrated with N/50-sodium hydroxide, required 3·7 ml. to the first phenolphthalein colour in the cold and at boiling temperature absorbed a further 5·88 ml. The titrated solution contained ionised iodine. Indicated equivalent weight, 131. $C_7H_{10}O_3I_2$ (VI) with loss of both iodine atoms requires 131·6.

The crude iodo-acid (VI) (0·17 g.) in ethanol (20 ml.) was titrated at boiling temperature with N/10-sodium hydroxide. Decolourisation of the indicator ceased when 12 ml. had been absorbed. The titrated solution was added to a suspension of palladium–charcoal catalyst and shaken under hydrogen until uptake ceased. The hydrogenated solution was evaporated under 15 mm. to one-third volume, acidified to Congo-red with sulphuric acid, and extracted with ether (100 ml. in four portions). The extract was thoroughly dried over sodium sulphate, and the solvent distilled off to leave a small residue of oil requiring 3·8 ml. of N/10-sodium hydroxide for neutralisation to pH 6·5. The resultant sodium salt was converted into a S-*benzylthiuronium* salt. Crystallised and recrystallised from freshly distilled methyl ethyl ketone, it separated in colourless laminæ, m. p. 144·5—145·5° [Found: C, 58·5; H, 7·0; N, 9·2; S, 10·7. $C_{15}H_{22}O_3N_2S$ (cf. VII) requires C, 58·1; H, 7·1; N, 9·0; S, 10·3%].

The *S*-benzylthiuronium salt of γ-keto-β-methylhexoic acid was prepared synthetically for comparison. Ethyl 2-keto-1-methyl-*n*-butylmalonate, b. p. 91—93°/0·1 mm., was obtained in 60% yield by slightly modifying the method of Raistrick *et al.* (*loc. cit.*). The ester (7·0 g.) was hydrolysed with aqueous alkali, and the malonic acid decarboxylated by heating at 135°/12 mm. Two distillations of the product gave γ-keto-β-methylhexoic acid (3·0 g.), b. p. 142—143°/12 mm. The *S*-benzylthiuronium salt prepared from this acid had m. p. 145·5—146·5°. A mixture with the substance isolated from clavatin melted at 145—146·5°.

Our thanks are due to Dr. A. E. Gillam of Manchester University for measuring absorption spectra. We have to thank Dr. R. Klein and Miss J. L. Ward of our microbiological laboratories for their invaluable work in obtaining the mould metabolites. The microanalyses were carried out by Drs. Weiler and Strauss. Technical assistance was given by Misses Gillman and Kuffall, Mrs. Etter and Mr. Lincoln.

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113. *The Formation of Azo-compounds from o-Nitrothiophenol and its Methyl Ether.*

By Charles Simons and L. G. Ratner.

o-Nitrothiophenol can be converted into azobenzene-2 : 2′-disulphinic acid (*sodium* salt) in the presence of sodium amyloxide at 130°. The methyl ether of the thiophenol under similar conditions gives a mixture of reduction products, with no oxidation of the sulphur atom.

It is well known that nitrobenzene can act as an oxidising agent in the presence of alkali; *e.g.*, *iso*eugenol is thereby converted into vanillin, the nitrobenzene being reduced to aniline with some azobenzene (E.P. 271818/9; *B.*, 1928, 360). Scholl (*Monatsh.*, 1913, **34**, 1011) discusses the intramolecular oxidation–reduction of *o*-nitrotoluene to anthranilic acid, suggesting a mechanism for the reaction and pointing out the difference between the *o*- and the *p*-isomer in their behaviour in this respect. Schönberg and Iskander (J., 1942, 90) describe the formation of 4 : 4′-azobenzaldehyde from α-(*p*-nitrobenzylthio)acetic acid and, like Scholl, postulate the formation of the enol form of the nitro-group before the reduction.

We have heated *o*-nitrothiophenol to 130° with sodium amyloxide in amyl alcohol. The resulting pink product indicated that the reaction had stopped at the azo-stage and was probably *sodium azobenzene-2 : 2′-disulphinate* as shown by analysis and ultra-violet absorption spectrum ($\log_{10}\varepsilon$ 4·27, 4·22, 2·27; $\lambda_{max.}$ 3270, 2250, 4650 A.). Fromm (*Ber.*, 1908, **41**, 3404) obtained *p*-nitrophenyl benzyl sulphide and *p*-nitrophenylsulphinic acid by heating dinitrodiphenyl disulphide with alkali and benzyl chloride, but Price and Twiss (J., 1910, **97**, 1175) could not get a sulphinic acid by similar means from diphenyl disulphide.

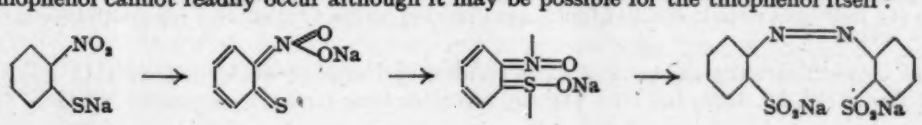
Our pink sodium salt, which is readily soluble in water, was acidified to give a pink acid, which gave two *esters* (probably dimorphous) with diazomethane ($\log_{10}\varepsilon$ 4·27, 4·28, 2·53; $\lambda_{max.}$ 2390, 3310, 4600 A.; $\log_{10}\varepsilon$ 4·26, 4·28, 2·53; $\lambda_{max.}$ 2400, 3330, 4600 A.) (cf. Cook, J., 1939, 1315). Both esters were readily hydrolysed by alkali.

Attempted reductions of the sulphinic acid to the known *o*-aminobenzenesulphinic acid (Claasz, *Annalen*, 1911, **380**, 309) failed, but the following observations were recorded. Acid reduction (zinc in acetic acid, zinc or tin and hydrochloric acid, etc.) gave colourless solutions but no substance corresponding in properties to *o*-aminobenzenesulphinic acid was isolated, owing perhaps to the ease with which the sulphinic group can be reduced to the thiophenol under such conditions. Bauer (*Annalen*, 1885, **229**, 368) attempted to reduce azobenzene-4 : 4′-disulphinic acid, finding that stannous chloride seems to give the hydrazo-compound but that sodium amalgam has no effect.

Alkaline reductions (zinc and ammonia or sodium hydroxide, sodium hyposulphite, or electrolytic) gave colourless or straw-coloured solutions, gradual acidification of which produced intense purple colours and then precipitated an orange acid, apparently different from the foregoing pink acid. Neither acid had definite characteristics. The methyl esters were rapidly hydrolysed on attempted alkaline reductions, and acid reductions gave colourless solutions from which no compound having the expected properties was isolated.

It was thought that a similar treatment of the methyl ether of *o*-nitrothiophenol with sodium amyloxide should give the corresponding azobenzenebismethylsulphone and this could be characterised by reductive fission of the azo-group to the known *o*-aminophenylmethylsulphone (Zincke and Siebert, *Ber.*, 1915, **48**, 1246). On treatment as before, a brick-red substance was obtained, which could be separated by chromatographic analysis into the red *azobenzene-2 : 2′-di(methylsulphide)* ($\log_{10}\varepsilon$ 4·35, 4·33, 4·06, 3·95; $\lambda_{max.}$ 2250, 2670, 3240, 4300 A.) (cf. Brand, *Ber.*, 1909, **42**, 3466) and the orange *azoxybenzene-2 : 2′-di(methylsulphide)* ($\log_{10}\varepsilon$ 4·45, 3·86; $\lambda_{max.}$ 2470, 3150 A.), identified by reduction to the colourless hydrazo-compound (Brand, *loc. cit.*), which was oxidised by heating in the air to the red azo-compound. Furthermore, after alkaline extraction of the aliphatic acids (formed by oxidation of the amyl alcohol) from the mother-liquors of the original reaction mixture, acid extraction gave a solution which when made alkaline afforded *o*-anisidine.

Contrary both to Scholl and to Schönberg and Iskander, enolisation of the nitro-group of the methyl ether of *o*-nitrothiophenol cannot readily occur although it may be possible for the thiophenol itself:



This would account for the exclusive formation of the azo-compound. In the case of the methyl ether, three reduction products were isolated, the azoxy-compound in the greatest yield. Furthermore, enolisation of the ether is not possible by the postulation of any intermediate compound capable of giving the compounds formed. It is known that nitrobenzene does not form an *aci*-salt and yet is capable of the oxidation of *iso*eugenol. The methyl ether may react in an analogous fashion.

Experimental.

o-Nitrothiophenol.—97 G. of di-*o*-nitrophenyl disulphide (m. p. 195°) were prepared and reduced by Claasz's methods (*Ber.*, 1912, **45**, 133, 2426) to give 60 g. of *o*-nitrothiophenol, m. p. 45°.

Dimethyl Azobenzene-2 : 2′-disulphinate.—12 G. of sodium were dissolved in 400 ml. of *n*-amyl alcohol under reflux, the solution heated to remove hydrogen, and cooled to 30—40°. 60 G. of *o*-nitrothiophenol were added, and the whole gently warmed in an oil-bath to 130°, whereupon a violent reaction set in and the flask was withdrawn from the bath. When the reaction had subsided it was completed by 30 mins.' heating. The mixture was cooled, filtered, and the residue washed with amyl alcohol, benzene, and finally petroleum. The crude substance (65 g.) was dissolved in hot methanol, filtered from inorganic salts, and evaporated to dryness. It recrystallised from water in spangles and was washed with methanol and ether; yield 20 g. of *sodium azobenzene-2 : 2′-disulphinate* (Found: C, 39·2; H, 3·1; S, 17·2; N, 7·7; Na, 11·9. $C_{12}H_8O_4N_2S_2Na_2$,MeOH requires C, 40·4; H, 3·1; S, 16·6; N, 7·3; Na, 11·9%. $C_{12}H_8O_4N_2S_2Na_2$,H_2O requires C, 38·7; H, 2·7; S, 17·2; N, 7·5; Na, 12·4%). The aqueous mother-liquors gave a buff-coloured solid (10 g.) which was mainly inorganic but contained a trace of diazotisable material.

1 G. of this sodium salt was acidified, sucked dry on a filter, suspended in 80 ml. of acetone–ether (1 : 1), and treated with diazomethane (from 2 g. of nitrosomethylurea). The solution was evaporated to dryness, the residue dissolved in benzene, treated with alumina, and fractionally crystallised, giving 0·7 g. of red needles, sparingly soluble in ethanol, m. p. 195° from acetone (Found: C, 50·1; H, 4·5; N, 8·8; *M*, Rast, 360. $C_{14}H_{14}O_4N_2S_2$ requires C, 49·7; H, 4·2; N, 8·3%; *M*, 338), and 0·3 g. of red rhombs, m. p. 135° from ethanol (Found: C, 50·2; H, 4·3; N, 8·7%; *M*, Rast, 363).

o-Nitrothiophenol Methyl Ether and its Reduction.—23 G. of *o*-nitrothiophenol were dissolved in 115 ml. of 2N-sodium hydroxide and 300 ml. of water, filtered from disulphide, and shaken with 10 ml. of methyl sulphate. After standing for 30 mins., the ether was filtered off; yield 20 g., m. p. 62—63° (Brand, *loc. cit.*). 20 G. of this methyl ether were reduced as above with 4·0 g. of sodium in 150 ml. of amyl alcohol. The red substance formed was filtered off, dissolved in benzene, washed with water, and dried over sodium sulphate. The benzene solution was poured on an alumina column, which was washed with benzene until the red band had been eluted and left the orange band, which was eluted with ethanol. The red band gave 2 g. of *azobenzene-2 : 2′-di(methylsulphide)*, m. p. 153—155°, from alcohol (Found: C, 61·65; H, 5·3; N, 10·0; S, 23·5. $C_{14}H_{14}N_2S_2$ requires C, 61·3; H, 5·15; N, 10·2; S, 23·4%). The orange band gave 8 g. of *azoxybenzene-2 : 2′-di(methylsulphide)* as orange needles from methanol, m. p. 78—80°, depressed by *o*-nitrothioanisole (Found: C, 57·8; H, 4·9; N, 9·8; S, 22·2. $C_{14}H_{14}ON_2S_2$ requires C, 57·9; H, 4·9; N, 9·7; S, 22·1%).

1 G. of the azoxy-compound was reduced in 50% alcohol by sodium hyposulphite to give colourless prismatic needles (from alcohol) of hydrazobenzene-2 : 2′-di(methylsulphide), m. p. 99—101°. Heated above its m. p. in air, this gave red plates, m. p. 155°, mixed m. p. with azobenzene-2 : 2′-di(methylsulphide) 155—156°. Reduction with zinc and sodium hydroxide or acetic acid gave the same hydrazo-compound.

The amyl alcoholic mother-liquors were washed with water and then alkali to remove fatty acids, and again with water. Extraction with dilute acid afforded a solution which, on being neutralised and steam-distilled, gave *o*-thioanisidine as an oil; b. p. 242°/760 mm., 134°/25 mm. Its picrate had m. p. 158° (from methanol) and, mixed with benzthiazole picrate (m. p. 169°), m. p. 148°; its acetyl derivative had m. p. 102—103°.

Attempted Preparation of o-Aminobenzenesulphinic Acid.—(*a*) 8 G. of sodium azobenzene-2 : 2′-disulphinate were treated with 4·5 g. of zinc, 4 g. of sodium hydroxide, and 25 ml. of water. The colourless solution was filtered, and on acidification it became purple, then pink, and finally deposited an orange-coloured acid of indefinite m. p., but giving a red solution in sodium hydroxide.

(*b*) Similar properties were shown by the product of an electrolytic reduction of 0·5 g. of the sodium salt in 10 ml. of N-sodium carbonate in a stone cell of 2 cm. diam. at 50° with a current of 5 volts and 0·8 amp., a platinum anode and a mercury cathode being used with an outer solution of 2N-sodium carbonate. (*c*) Sodium hyposulphite, sodium sulphite, sodium sulphide, titanous chloride, zinc in ammonia, and aluminium amalgam with ether (*d* 0·720), hot water, or 95% alcohol all gave the same sort of product. (*d*) Tin and hydrochloric acid with or without acetic acid gave colourless solutions not containing the required compound. (*e*) Zinc and hot glacial acetic acid gave a colourless solution from which extracts were obtained which diazotised and seemed to be of the aminothiophenol type. (*f*) Zinc and ethanolic hydrogen chloride behaved similarly. (*g*) The methyl esters, m. p. 195° and 135°, also failed to give the required product with sodium hyposulphite, or zinc with sodium hydroxide or acetic acid.

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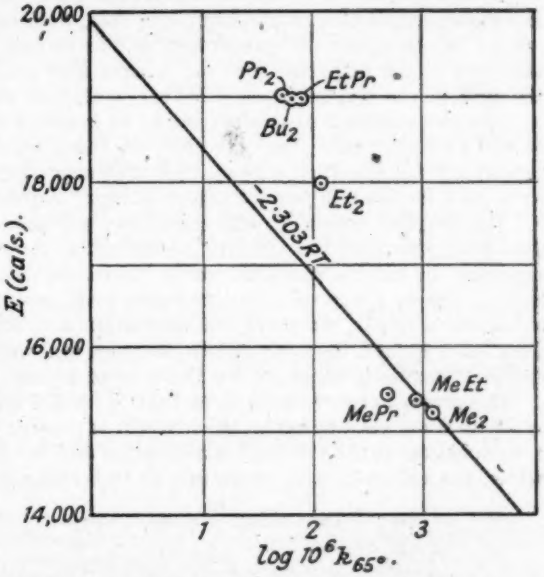
114. *The Influence of Alkyl Groups upon Reaction Velocities in Solution. Part V. The Formation of Phenyltrialkylammonium Iodides in Methyl Alcohol.*

By David P. Evans.

A study of the reactions between several dialkylanilines and methyl iodide has shown that in passing from methylalkylanilines to diethyl-, ethylpropyl-, dipropyl-, or dibutyl-aniline there is a large increase in activation energy accompanied by a rise in the factor *PZ* of the kinetic equation. The observations have been interpreted as being due mainly to a steric effect of the terminal methyl groups coupled with the possible formation of a hydrogen bond.

The reaction between tertiary amines and alkyl halides, first studied by Menschutkin (*Z. physikal. Chem.*, 1890, **6**, 41; *Ber.*, 1895, **28**, 1399, and later papers), has often been further investigated, but only Winkler and

Hinshelwood (J., 1935, 1147), Laidler (J., 1938, 1786), Evans, Watson, and Williams (J., 1939, 1345, 1348), and Brown and Fried (*J. Amer. Chem. Soc.*, 1943, **65**, 1841) have provided data suitable for analysis on the basis of the kinetic equation $k = PZe^{-E/RT}$, which affords useful indications of the effects of the substituents upon reactivity. As an extension of the problem indicated in the title, the reaction between methyl iodide and several dialkylanilines has been studied at various temperatures in methyl alcohol as solvent. Some of the preliminary results have been quoted elsewhere (*Trans. Faraday Soc.*, 1941, **37**, 645) but now circumstances make it desirable to record the results and conclusions to date.



Experimental.

Materials.—The dialkylanilines were prepared by Hickinbottom's methods (J., 1930, 992) and in all cases were freed from traces of primary and secondary bases by treatment with acetic anhydride and subsequent steam distillation. The liquids boiled within 0·1° of the temperatures recorded: Me_2, 95°/30 mm.; Et_2, 96°/13 mm.; Pr^n_2, 122°/14 mm.; *n*-Bu_2, 130°/7 mm.; MeEt, 89·5°/15 mm.; $MePr^n$ 96·5°/10 mm.; $EtPr^n$, 111°/13 mm.

Measurements.—The reactions were carried out at three temperatures in absolute methyl alcohol exactly as described by Evans, Watson, and Williams. Satisfactory velocity constants were obtained by applying the simple bimolecular formula in the case of dimethyl-, methylethyl-, methylpropyl-, and dibutyl-anilines, but the other compounds showed slight autocatalysis. In these cases the slope of the tangent at zero time to the curve obtained on plotting $1/(a - x)$ against time gave constants which fell on the Arrhenius line. The tangents always passed through the first one or two points recorded and extrapolation of the plot of k against percentage change also gave the same values of the velocity coefficients. A typical set of results is recorded below, where a = initial concentration of amine and iodide, x = concentration of the quaternary salt, and k is the velocity coefficient in l. g.-mol.$^{-1}$ sec.$^{-1}$.

Methylethylaniline and methyl iodide at 44·85°.

a = 0·09754 g.-mol. per litre.

Time (mins.)	125	255	390	565	890	990	1140	1320
Titre, c.c. of 0·0113N-$AgNO_3$	4·49	7·94	10·9	13·85	17·75	18·75	19·80	21·30
10^4k	2·00	1·95	1·96	1·96	1·96	1·96	1·93	1·98

The following table records the results for the velocity coefficients at various temperatures, together with the calculated values of the energies of activation and of log PZ.

Dimethylaniline.		Methylethylaniline.		Methyl-*n*-propylaniline.		Diethylaniline.	
Temp.	10^4k.	Temp.	10^4k.	Temp.	10^4k.	Temp.	10^4k.
25°	0·562	44·85°	1·97	44·8°	1·12	65°	1·24
35·5	1·31	65	8·50	65·25	4·94	85·5	5·69
65	11·9	84·2	29·0	84·9	17·5	99·4	14·9
E = 15,200		E = 15,400		E = 15,430		E = 18,000	
log PZ = 6·9		log PZ = 6·9		log PZ = 6·7		log PZ = 7·7	

Ethyl-*n*-propylaniline.		Di-*n*-propylaniline.		Di-*n*-butylaniline.	
65	0·775	65·2	0·548	65	0·68
84·3	3·54	84·7	2·52	85	2·83
99·8	11·0	100	7·72	100	8·66
E = 19,030		E = 19,060		E = 19,000	
log PZ = 8·2		log PZ = 8·1		log PZ = 8·1	

Discussion.

The velocity coefficients at 65° decrease in the order Me_2 > MeEt > MePr > Et_2 > EtPr > Pr^n_2; an approximately constant value being attained in the dipropyl compound. The velocity coefficients at 65° referred to that of dimethylaniline as unity are given in the second line below:

	Aniline.	Me_2.	MeEt.	MePr.	Et_2.	Pr^n_2.
k_{R_2}/k_{Me_2}	Present work	1·0	0·71	0·41	0·10	0·046
	Thomas	1·0	0·66	0·44	0·07	—

and are in close accord with the same ratios (third line) calculated from Thomas's results (J., 1913, **103**, 594) for the reaction of these bases with allyl bromide at 40° in ethyl alcohol. The similarity appears to indicate that, although the absolute values of the coefficients in the two reactions differ in the ratio of *ca.* 10^3, the variation in velocity from base to base is independent of the alkyl halide and is governed by the nature of the alkyl groups in the base.

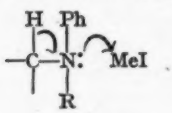
The formation of quaternary ammonium salts is facilitated by electron accession at the nitrogen atom (cf. Davies and Lewis, J., 1934, 1599; Evans, Watson, and Williams, *loc. cit.*); the increase in velocity due to an electron-repulsive *m*- or *p*-nuclear substituent being caused entirely by the decrease in activation energy. Hinshelwood, Laidler, and Timm (J., 1938, 848) have suggested that, since both the basic strength and the energy of activation for quaternary salt formation appear to be governed by the reactivity of the unshared electrons of the nitrogen, then for a given alkyl halide the activation energy should increase with decreasing strength of the tertiary base. Several instances were quoted by these workers where this rule was obeyed; *e.g.*, for the addition of methyl iodide to pyridine and triethylamine (in benzene) the activation energies are 14,300 and 9700 cals., respectively. In the dialkylanilines the slight increase in the inductive effect of the substituents as the alkyl series is ascended might be expected (in the absence of any other complicating effects) to cause a decrease in the activation energy; experiment, however, proves that this is not the case.

The detailed results (p. 423) show that, whenever the tertiary base contains two groups higher than methyl linked to nitrogen, the velocity coefficient is lower than that for the methylalkylanilines. This would be expected on the conventional steric hindrance effect. When the energies of activation are plotted against log $k_{65°}$ (see fig.), however, in agreement with most recent work it is found that the decrease in velocity is due mainly to a rise in the energy of activation and not to a fall in the non-exponential factor of the kinetic equation; in fact, there is a general increase in P with E as the alkyl chain lengthens. A possible reason for this rise in P has been suggested by Davies and Evans (J., 1940, 339) and Evans, Watson, and Williams (*loc. cit.*).

The present observations show that the slight increase in the normal inductive effect of the alkyl groups is offset by some very powerful effect which is present in all the bases containing two groups higher than methyl. A comparison of the energies of activation and the base strengths is instructive. The relevant data are given below, the values of pK_B being due to Hall and Sprinkle (*J. Amer. Chem. Soc.*, 1932, **54**, 3469).

Alkyl subst.	Me_2.	MeEt.	Et_2.	MePr.	EtPr.	Pr_2.
pK_B	5·06	5·98	6·56	5·64	6·34	5·57
E, cals.	15,200	15,400	18,000	15,430	19,030	19,060

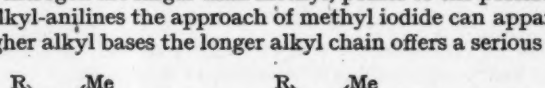
Even in the base strengths the influence of the inductive effect of the alkyl groups does not offer a complete interpretation, since the ethyl substituent has a definite enhancing influence not present in methyl or *n*-propyl. On passing from dimethylaniline to the stronger bases diethyl-, dipropyl-, or ethylpropyl-aniline, the activation energies for the addition of methyl iodide *increase* by a considerable amount (3000 cals. approx.) instead of decreasing as expected on the suggestion of Hinshelwood, Laidler, and Timm, whilst for the methylalkylanilines, which vary appreciably in strength, the activation energies are practically constant. It follows that in the present case there must be an important factor other than the availability of the unshared electrons on the nitrogen atom. The actual nature of this effect, which becomes sharply evident in the diethyl member, is not easy to determine and the following are possible interpretations. Baker (*Trans. Faraday Soc.*, 1941, **37**, 647) has suggested that the increase in activation energy in the diethyl and higher dialkylanilines may be due to the decreased electron release according to the mechanism (I) occurring in the transition complex.



(I.)

Since the alkyl group is so close to the seat of the reaction, such an effect might have a large influence on the activation energy. It is difficult, however, to understand why it is essential to have substitution in both the methyl groups of dimethylaniline before the influence is felt.

Brown and Fried (*loc. cit.*) have recently put forward an interesting suggestion regarding the influence of retarding ortho-substituents in the Menschutkin reaction, which closely resembles a postulate of Hughes (*Trans. Faraday Soc.*, 1941, **37**, 620) in connection with the bimolecular hydrolysis of *neo*pentyl bromide. Brown and Fried suggest that in quaternary salt formation "the alkyl group approaches the exposed face of the nitrogen atom along a line at right angles to the plane of the three groups to which it is attached. In hindered amines the nitrogen atom is shielded from approach along a normal line." The sudden large increase in activation energy (approx. 5000 cals.) in passing from $n = 3$ to $n = 4$ in $C_6H_4{\cdot}[CH_2]_n{\cdot}NMe$ supports this view. The similar sudden large increase in E found in the present work when both groups attached to nitrogen are larger than methyl, points to the possibility of a similar explanation. In dimethyl- and the methylalkyl-anilines the approach of methyl iodide can apparently take place unhindered (II), but in the diethyl and higher alkyl bases the longer alkyl chain offers a serious obstruction to the approach-

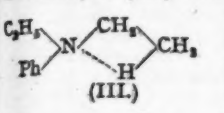


(II.)

ing methyl. Here we have an almost pure bulk effect which appears similar to that observed in the bimolecular hydrolysis of *neo*pentyl bromide (Hughes, *loc. cit.*), the sudden rise in E being expected because of the steep rise in the potential-energy curves when the distance between the terminal methyl groups of the substituents and the attacking reagent falls below a critical value.

The third possible explanation of the rise in activation energy observed here is an extension of the suggestion given in previous parts of this series, *viz.*, the possibility of hydrogen-bond formation in the transition complex between the alkyl group and the reactive centre of the molecule. In diethylaniline, ring formation of the type

indicated in (III) would involve formation of a 4-membered " ring " which might exist in the transition state of the reaction with methyl iodide. The constraint thus placed on the nitrogen lone pair would possibly account for the rise in activation energy in passing from dimethyl- to diethyl-aniline. The further rise in E for dipropyl-, ethylpropyl-, and dibutyl-anilines may be accounted for by the formation of more stable five- and six-membered rings by hydrogen-bond formation between the terminal methyl and the nitrogen, which involves greater restraint on the unshared electrons.



(III.)

Which of these interpretations is nearest the truth it is difficult to decide. In any reaction each effect may come into play simultaneously with one preponderating over the other two. The author regards the second interpretation as the most likely in the present case, with the possible intervention of the hydrogen bond as a supporting effect. It would be interesting to discover whether, on increasing the size of the entering group, the steric influence due to repulsion as suggested by Hughes and by Brown and Fried would be felt in methylpropyl- or even methylethyl-aniline.

The author expresses his grateful thanks to Dr. R. Williams for his help in some of the measurements, and to Dr. H. B. Watson for his continued interest.

TECHNICAL COLLEGE, CARDIFF. [*Received, April 27th*, 1944.]

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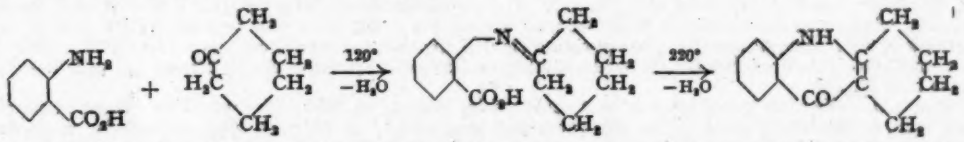
115. *Hydroacridones. Synthesis and Dehydrogenation.*

By R. A. REED.

The five methylanthranilic acids have been condensed with *cyclo*hexanone at 220°. Anthranilic acid has been condensed similarly with 2-methyl*cyclo*hexanone. The condensation product obtained by Perkin and Sedgwick (J., 1924, **125**, 2441) from anthranilic acid and 3-methyl*cyclo*hexanone is shown to be 2-methyl-1 : 2 : 3 : 4-tetrahydroacridone by its dehydrogenation to 2-methylacridone. All these methyltetrahydroacridones have been dehydrogenated to the corresponding methylacridone by heating with copper in air at 360°.

THE hydroacridones, hitherto but little studied, provide a good method for the preparation and proof of configuration of the substituted acridones and acridines. Tiedkte (*Ber.*, 1909, **42**, 621) heated *cyclo*hexanone with anthranilic acid at 120°, obtaining an anil, easily soluble in both acids and alkalis, and further heating at 220° afforded 1 : 2 : 3 : 4-tetrahydroacridone in 40% yield.



That anil formation is not essential for the subsequent formation of the tetrahydroacridone is shown by the fact that *N*-methylanthranilic acid condenses readily with *cyclo*hexanone to form *N*-methyl-1 : 2 : 3 : 4-tetrahydroacridone. In any case no anil was isolated by condensation at 120° of the four *C*-methylanthranilic acids, the only solid product being unchanged acid. Condensation at 220°, however, readily afforded methyl-1 : 2 : 3 : 4-tetrahydroacridones.

Hughes and Lions (*Proc. Roy. Soc. N.S.W.*, 1937, **71**, 458) prepared tetrahydroacridones by condensing primary aromatic amines with ethyl *cyclo*hexanone-2-carboxylate at room temperature with hydrogen chloride as catalyst, obtaining anils which were subsequently cyclised by being heated to 100° and added to liquid paraffin at 280°. In this way they prepared 7- and 9-methyl-1 : 2 : 3 : 4-tetrahydroacridones, both melting above 300°.

The hydroacridones now reported are high-melting solids, best recrystallised from pyridine. They show no fluorescence in alcoholic solution in daylight but are, with one exception, fluorescent under ultra-violet light, giving different colours or intensities of light under acid and alkaline conditions. Their solutions in cold concentrated sulphuric acid are yellow, without daylight fluorescence. These liquids when poured into 10 volumes of water produce clear, colourless solutions, evidence of the basic nature of these compounds.

The compounds are soluble in alcoholic alkali (the *N*-methyl member by virtue of its solubility in alcohol alone) but not in aqueous alkali. They also readily dissolve in 5N-hydrochloric acid, some yielding crystalline hydrochlorides on cooling. These hydrochlorides are hydrolysed by water but are stable in very dilute hydrochloric acid. All the hydrochloride solutions yield a precipitate of the corresponding dichromate on addition of *excess* of potassium chromate solution.

The hydroacridones, like the hydrocarbazoles, yield picrates from acetic acid which possess sharp melting points.

On heating with copper powder in air at 360° the tetrahydroacridones lose hydrogen, passing into the corresponding acridone. This method is the cleanest and best yet tried, being preferable to heating with lead oxide (von Braun and Wolff, *Ber.*, 1922, **55**, 3676), heating alone in air at 280° (Tiedkte, *loc. cit.*), or heating with sulphur in quinoline solution (Perkin and Plant, J., 1923, **123**, 694), the last method producing from tetrahydroacridone itself a substance containing sulphur which is not thioacridone.

Experimental.

All the corrected m. p.'s given were obtained in a liquid-paraffin bath. For m. p.'s well above 300°, the bath was heated at such a rate that a temperature of 300° was reached in 5 minutes. Heating was then continued at the normal rate.

1 : 2 : 3 : 4-*Tetrahydroacridone*.—A mixture of 2 g. of *cyclo*hexanone (94%, 1·3 mols.) and 2 g. of anthranilic acid was heated with occasional stirring to 220° during 1 hour and kept at 220—240° for 30 mins. To the warm residue were added 15 ml. of benzene, the mixture refluxed for 30 mins., and allowed to cool. After being filtered off, the solid was washed with benzene until the filtrate was colourless, and finally with ether, and dried in air. The cream-coloured solid was recrystallised from pyridine, giving colourless needles, m. p. 370° (Tiedkte, *loc. cit.*, gives 358°). The yield of crude product was 1·8 g. (60%). Titration of the picrate (m. p. 198°) to *m*-cresol-purple with 0·1N-sodium hydroxide gave for the base *M*, 202·5 (Calc. for $C_{13}H_{13}ON$: *M*, 199).

9-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—Prepared as above from 2 g. of 3-methylanthranilic acid (made as in D.R.-P. 375,616; see also *Org. Synth.*, 1925, **5**, 71; *Arch. Pharm.*, 1929, **267**, 578) and 2 g. of *cyclo*hexanone (94%, 1·5 mols.), this *compound* was obtained in a yield of 1·8 g. (64%); recrystallisation from pyridine gave colourless needles, m. p. 346° (Found: N, 6·3. $C_{14}H_{15}ON$ requires N, 6·6%). The picrate separates from acetic acid as yellow needles, m. p. 215—216°.

8-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—This compound was prepared from 2·2 g. of *cyclo*hexanone (94%) and 2 g. of 4-methylanthranilic acid (made essentially according to Niementowski, *J. pr. Chem.*, 1889, **40**, 1), the yield of solid, washed with alcohol in place of benzene, being 1·2 g. (42%); recrystallisation from pyridine gave cream-coloured plates, m. p. 378°. The *picrate* had m. p. 208—209° (Found, by titration: *M*, 441. $C_{14}H_{15}ON,C_6H_3O_7N_3$ requires *M*, 442).

7-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—2 G. of *cyclo*hexanone (94%) and 2 g. of 5-methylanthranilic acid (made as in D.R.-P. 375,616; see also *Org. Synth.* and *Arch. Pharm.*, *locc. cit.*), heated as above, gave 1·95 g. (69%) of the *acridone*; recrystallised from pyridine, this formed cream plates, m. p. 374° (Found: N, 6·4%). The picrate separates from acetic acid as yellow prisms, m. p. 194—196°.

6-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—7·8 G. of 6-methylanthranilic acid (m. p. 128—129°, decomp.; prepared as by Gabriel and Thieme, *Ber.*, 1919, **52**, 1079) and 10 ml. of *cyclo*hexanone (94%) were heated at 220° for 1½ hours, and the solid residue washed with alcohol; this afforded 3·9 g. (35%) of colourless prisms, m. p. 355°, purification being unnecessary. This compound, unlike the other methyltetrahydroacridones, shows no u.v. fluorescence in alcoholic solution under acid or alkaline conditions. The *picrate* had m. p. 165—185° (Found: *M*, 438·5).

2-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—One hour's heating of a mixture of 2 g. of anthranilic acid and 2·5 ml. of 3-methyl*cyclo*hexanone (98%) at 220° gave 2·4 g. (77%) of benzene-washed product; recrystallisation from pyridine yielded white to faintly pink leaflets, m. p. 362°. Titration of the *picrate* [m. p. 212° (decomp.) not raised by recrystallisation; 0·35 g. from 0·2 g. of each component] showed that the base had *M*, 210. The high yield of pure picrate indicates that only one of the two possible methyltetrahydroacridones was formed. Its configuration was proved by dehydrogenation to 2-methylacridone (see below).

1-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—A mixture of 20 g. of anthranilic acid and 25 g. of 2-methyl*cyclo*hexanone (93%), heated to 220° during 1½ hours and kept at 220° for a further 1½ hours, gave 15 g. (48%) of alcohol-washed product. Recrystallisation from pyridine yielded cream-coloured needles, m. p. 305°. Titration of the *picrate* (m. p. 183—184°) showed for the base *M*, 215.

10-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—A mixture of 10 g. of *N*-methylanthranilic acid (Houben and Brassert, *Ber.*, 1906, **39**, 3235; yield of pure acid 50%) and 12 ml. of *cyclo*hexanone (97·5%) after 3 hrs. at 220° gave a residue, solid when cold, which was recrystallised from benzene, giving 8·5 g. (60%) of pale yellow needles, melting over a wide range beginning at 86°; recrystallisation from pyridine yielded cream-coloured prisms, m. p. 170—172°. This compound, unlike the *C*-methyltetrahydroacridones, is easily soluble in alcohol. Titration of the *picrate* (m. p. 209—210°) showed that the base had *M*, 220.

Dehydrogenations.—Dehydrogenation was best achieved by heating at 360° with 2 parts by weight of copper powder, the mixture being intimately ground. The apparatus consisted simply of a Hirsch tube, as used for small-scale suction filtration, fitted with an inner boiling tube through which cold water was passed, to act as condenser. The mixtures were heated in a metal-bath at 360° for 30 minutes, the yellow sublimate removed by a long spatula, the residue reground and reheated at 360° for another ½ hour, and the procedure repeated once more. No more sublimate was obtained by a fourth period of heating. The combined sublimate was dissolved in a mixture of alcohol and 5N-sodium hydroxide and filtered hot. The acridone derivative separated on acidifying the filtrate with dilute hydrochloric acid, any unchanged tetrahydroacridone remaining in solution as the hydrochloride. After being cooled and filtered off, the yellow solid was recrystallised from a suitable solvent.

1 : 2 : 3 : 4-Tetrahydroacridone (2 g.) yielded 0·5 g. of pure acridone, m. p. 358° after recrystallisation from benzyl alcohol. A mixed m. p. with authentic acridone [prepared by cyclisation of *N*-phenylanthranilic acid (see *Org. Synth.*, 1939, **19**, 6) and purified as above] showed no depression.

2-Methyl-1 : 2 : 3 : 4-tetrahydroacridone (2 g.) gave 0·2 g. of 2-methylacridone; recrystallised from pyridine, the yellow needles had m. p. 337°. A mixed m. p. with 3-methylacridone, m. p. 338°, prepared from *p*-tolylanthranilic acid by cyclisation with concentrated sulphuric acid (Graebe and Kahn, *Annalen*, 1894, **279**, 272) gave a depression of 12°. The 8-methyl isomer (0·5 g.) gave 0·1 g. of 2-methylacridone, m. p. 342° (Bamberger, *Ber.*, 1909, **42**, 1719, gives m. p. 344°) after recrystallisation from alcohol; mixed m. p. with above 2-methylacridone, 339°, confirming the orientation of 2-methyl-1 : 2 : 3 : 4-tetrahydroacridone.

6-Methyl-1 : 2 : 3 : 4-tetrahydroacridone (1 g.) yielded 0·3 g. of 4-methylacridone, m. p. 318° (Gleu and Nitzsche, *J. pr. Chem.*, 1939, **153**, 219, give m. p. 315°) after crystallisation from aqueous alcohol. This methylacridone is much more soluble in hot alcohol than its three *C*-methyl isomers. A mixed m. p. determination with the product from 2-methyl-1 : 2 : 3 : 4-tetrahydroacridone gave a depression of 7°. It seems probable that 4-methylacridone was the isomer, m. p. 312°, obtained by Senier and Shepheard (J., 1909, **95**, 444) by dry distillation of salicyl-*m*-toluidide.

9-Methyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·15 g. of 1-methylacridone after recrystallisation from acetic acid. The yellow needles, m. p. 342°, gave no depression on mixing with a sample of authentic 1-methylacridone, m. p. 345°, prepared by cyclisation of *o*-tolylanthranilic acid (Graebe and Locher, *Annalen*, 1894, **279**, 279), but gave a depression of 11° with 2-methylacridone.

1-Methyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) yielded 0·1 g. of yellow needles, m. p. 342°, after recrystallisation from acetic acid, undepressed when mixed with authentic 1-methylacridone; and the 7-methyl compound (0·5 g.) yielded 0·2 g. of 3-methylacridone after crystallisation from acetic acid, m. p. and mixed m. p. 339°. The 10-methyl compound (0·5 g.) yielded 0·1 g. of *N*-methylacridone, m. p. 201°, after three crystallisations from alcohol (Graebe and Lagodzinski, *Annalen*, 1893, **276**, 47, give m. p. 203°); this compound is insoluble in cold alcoholic alkali.

Dimethyltetrahydroacridones and dihydrobenzacridones have also been prepared and dehydrogenated and this investigation will be reported in a later publication.

Research Laboratory, Hopkin and Williams, Ltd., London, E.C. 1. [*Received, April 28th*, 1944.]

116. *The Reduction of Quinaldinic Acid at the Dropping-mercury Cathode.*

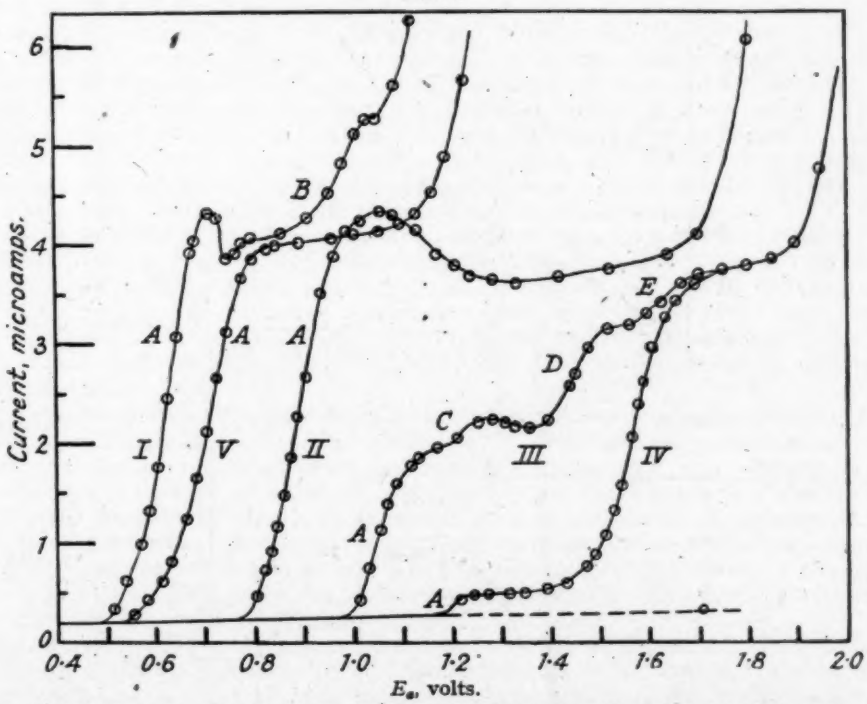
By JOHN T. STOCK.

Current–voltage curves of quinaldinic acid in well-buffered aqueous solutions of pH 1·5—12 have been constructed, reduction occurring over the entire pH range. The principal reduction product appears to be dihydroquinaldinic acid. Since the wave heights are proportional to the concentration of quinaldinic acid, this acid may be estimated polarographically.

THE systematic development of the technique of amperometric titration by means of the dropping-mercury electrode (see, *e.g.*, Kolthoff and Lingane, "Polarography," New York, 1941, pp. 447—478) indicated the utility of certain of the well-known organic precipitants for metallic ions in this connection. Quinaldinic acid, a reagent for the gravimetric determination of copper, zinc, and cadmium (Hopkin and Williams, Ltd., "Organic Reagents for Metals," 1943, pp. 122—125), has potential uses in this procedure, and the present work concerns its behaviour at the dropping-mercury cathode.

Current–voltage curves of quinaldinic acid (0·001M) in well-buffered aqueous solutions at 25° over the pH range 1·5—12 have been constructed. Müller (*Chem. Rev.*, 1939, **24**, 107) has stressed the importance of

FIG. 1.



Curve I, pH 1·50; *II*, pH 5·75; *III*, pH 7·91; *IV*, pH 10·69; *V, as I, but* 0·02% *gelatin added.*

adequate buffering in studying the electroreduction of organic compounds. Quinaldinic acid was found to be reducible over the entire pH range examined. In strongly acid solutions the first wave *A* (Fig. 1, curve I) is surmounted by a "maximum" and followed by a second, smaller wave *B* which immediately precedes the rapid rise in current due to the decomposition of the supporting electrolyte. Under these conditions quinaldinic acid, in common with other quinoline derivatives, decreases the overvoltage of hydrogen. As the pH of the solution is increased, wave *A* is displaced to more negative potentials, the maximum broadening considerably. At the same time, wave *B* decreases in height, vanishing completely at about pH 4 (Fig. 1, curve II). In the region of neutrality the current–voltage curves become very complicated, no less than four waves *A*, *C*, *D*, and *E* appearing (Fig. 1, curve III). Wave *C* can be distinguished in the pH range 6·4—8 and decreases in height with increase in pH. Its appearance coincides with a marked decrease in the height of wave *A*. Wave *D* appears at pH 5·5 and wave *E* at about pH 7·4. Both increase in height with increase in pH, the former merging into the latter in the region of pH 9. In solutions more alkaline than pH 9, wave *A* becomes very small (Fig. 1, curve IV). It is, however, still distinguishable at pH 12·3. In 0·1M-sodium hydroxide solution it was not observed.

The reduction potential of wave *A* as determined by the "45° tangent" method (Heyrovsky, *Coll. Czech. Chem. Comm.*, 1935, **7**, 198) is displaced to more negative potentials with increase in pH. Up to pH 5, this displacement is linear, the reduction potential being given by $E = -(0{\cdot}42 + 0{\cdot}06\ \mathrm{pH})$ volt. All potentials are referred to the saturated calomel electrode at 25°.

To permit analysis of the results, attempts were made to suppress the maximum surmounting wave *A*. Methyl-red and methylene-blue fail completely, even when added in concentrations large enough to increase the residual current considerably. Thymol is also ineffective. The maximum is completely suppressed by the addition of 0·02% of gelatin, but at the same time wave *A* is displaced to a more negative potential range, while wave *B* is completely eliminated (Fig. 1, curve V). The lateral displacement of wave *A* is similar to the effect observed by Kolthoff and Barnum (*J. Amer. Chem. Soc.*, 1941, **63**, 521) in their work on cystine. Applic-

FIG. 2.

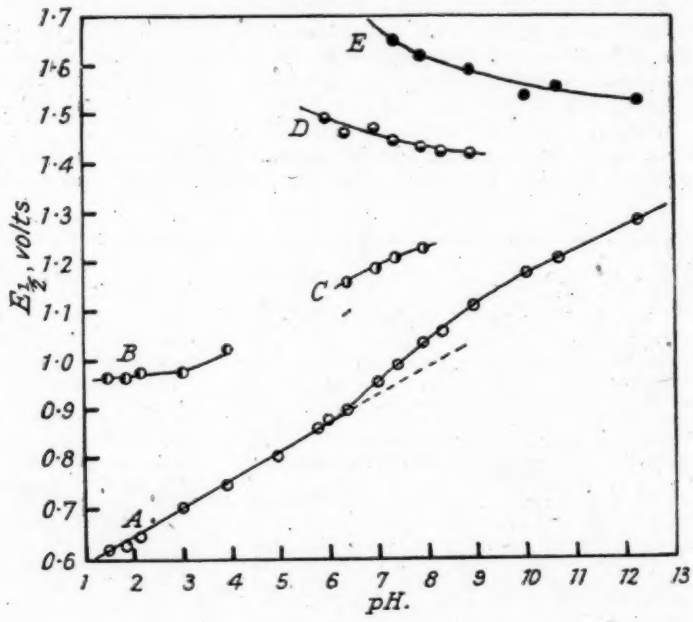


FIG. 3.

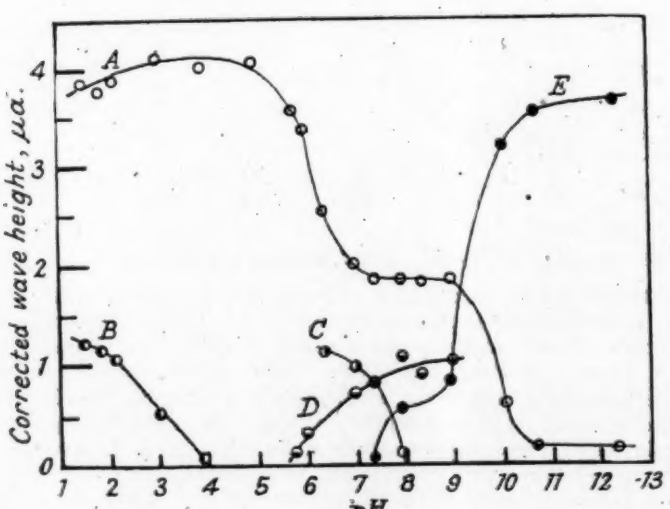
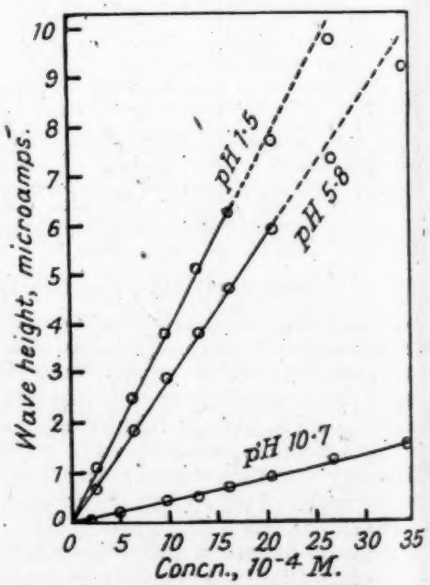


FIG. 4.



ation of the wave heights measured in the presence of gelatin to the corresponding curves obtained in its absence permits a fair estimate of the half-wave potentials ($E_{\frac{1}{2}}$). Up to pH 6 the relation $E_{\frac{1}{2}} = -(0{\cdot}52 + 0{\cdot}06\ \text{pH})$ volt holds for wave *A*. No maximum suppressor is necessary with solutions of pH >7. Fig. 2 shows the $E_{\frac{1}{2}}$–pH relationships of the various waves, constructed directly from current–voltage curves obtained in the absence of gelatin (except in the case of wave *A* up to pH 7, when the method described was used).

The magnitude of the waves also depends markedly on pH, as is shown by Fig. 3. The wave heights are corrected both for the residual current of the supporting solution and for the varying drop-time of the capillary

due to the occurrence of the waves at different potentials (Lingane and Kolthoff, *J. Amer. Chem. Soc.*, 1939, **61**, 831). The heights of wave *A* up to pH 7 are those recorded after the addition of gelatin; other measurements were made in the absence of this agent.

Though the effect of pH on wave *A* is remarkable, the wave height is directly proportional to the concentration of quinaldinic acid in buffers of widely differing pH. As shown in Fig. 4, this relationship holds for concentrations up to 2×10^{-3}M. (Wave heights here are corrected for residual current only.) Accordingly, the measurement of the height of wave *A* provides a means of estimating quinaldinic acid polarographically. The total wave height in alkaline solution, *viz.*, the sum of the heights of waves *A* and *E*, is also proportional to the concentration. At concentrations $>2 \times 10^{-3}$M, in the presence of gelatin, the rising portion of wave *A* is seen to be composite, the lower half being steeper than the upper half. $E_{\frac{1}{2}}$ becomes slightly less negative with increasing concentration of quinaldinic acid, probably due to the displacing effect of the constant concentration of gelatin being partly counteracted.

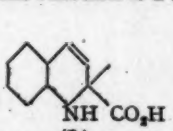
To permit application of Ilkovič's equation (*Coll. Czech. Chem. Comm.*, 1934, **6**, 498), the diffusion coefficient (D) of the quinaldinate ion was calculated from the relation $D = \boldsymbol{R}T\Lambda_0/zF^2$, where Λ_0 is the equivalent conductance of the ion at infinite dilution and z its valency (Lingane and Kolthoff, *loc. cit.*, p. 825). Use of the data due to Ostwald (*Z. physikal. Chem.*, 1889, **3**, 369; International Critical Tables, **6**, 293) in the above equation gives $D = 0{\cdot}80 \times 10^{-5}$ cm.^{2} sec.$^{-1}$ at 25°.

Ilkovič's equation is usually expressed as $I_d = 605nD^{\frac{1}{2}}Cm^{2/3}t^{1/6}$, where I_d is the diffusion current (wave height) in microamps., n the number of electrons involved per mol., C the concentration (in millimols./l.), m the rate of flow of mercury from the capillary (in mg./sec.), and t the drop time (in secs.). By applying this equation to wave *A* at pH 5 (at which value no other waves are detectable, see Fig. 3), n was found to be 2·05. Since quinaldinic acid is incompletely ionised under these conditions, this result is an approximation, but is sufficient to show that wave *A* at its fullest development corresponds with a reduction involving 2 electrons per mol. In 0·1M-sodium hydroxide solution, *E* is the only wave detectable. Application of Ilkovič's equation here yields the value $n = 1{\cdot}96$. Hence wave *E* also corresponds with a 2-electron reduction.

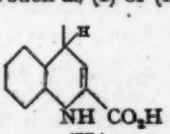
Discussion.—The reduction of quinoline at the dropping-mercury cathode has been studied by Pech (*Coll. Czech. Chem. Comm.*, 1934, **6**, 126), by Tachi and Kabai (*J. Electrochem. Assoc. Japan*, 1935, **3**, 250; *Chem. Abstracts*, 1936, **30**, 2500) and by Adkins and Cox (*J. Amer. Chem. Soc.*, 1938, **60**, 1151). In neutral and alkaline solution Pech reported two waves of equal height which he attributed to the formation of dihydro- and tetrahydro-quinoline severally. According to the Japanese workers the reduction product is dihydroquinoline. Apart from quinine (Pech; Tachi and Kabai, *locc. cit.*), no derivatives of quinoline have been examined polarographically.

Interpretation of the results is rendered difficult by the known tendency to polymerisation of dihydroquinoline and its derivatives. According to Meerwein (Houben's "Die Methoden der organischen Chemie," Leipzig, 1925, **2**, 620), only the *N*-substituted derivatives are known in the monomeric form. Ahrens (*Z. Elektrochem.*, 1896, **2**, 580) studied the electrolytic reduction of quinoline and quinaldine in sulphuric acid solution using a lead cathode and obtained monomeric, dimeric, and trimeric dihydro-compounds. Levchenko (*J. Gen. Chem., U.S.S.R.*, 1941, **11**, 686) further studied the reduction of quinoline in alkaline solution, using a mercury cathode. He reported a 30% yield of trimeric 1 : 4-dihydroquinoline with smaller amounts of the monomeric and the dimeric form. In sulphuric acid solution the trimer only was obtained. Accordingly, the reaction products discussed below may, in fact, exist in polymerised forms.

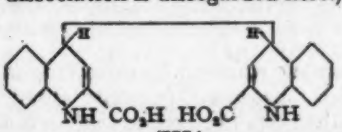
The step-like form of the pH–wave height curve of wave *A* (Fig. 3) is peculiar. In accordance with the composite appearance of this wave in acid solution, logarithmic analysis (Kolthoff and Lingane, *op. cit.*, p. 144) under these conditions gives a curve which is linear over the portion corresponding to the lower half-wave, but which deviates markedly beyond this. The occurrence of two reactions at potentials very close to one another is a possible explanation. Since on increasing the pH, wave *C* appears as the height of wave *A* shows a marked decrease, it seems that the composite wave splits up into its components due to the increased separation of the two reduction potentials. The constant height of wave *A* over the pH range 7·5—9 yields a value $n = 0{\cdot}95$ when inserted into Ilkovič's equation, corresponding to a one-electron reaction which is probably reversible, since logarithmic analysis yields linear curves of reciprocal slope 0·064 (cf. Laitinen and Wawzonek, *J. Amer. Chem. Soc.*, 1942, **64**, 1765). Since $E_{\frac{1}{2}}$ varies with pH, hydrogen ions are involved in the electrode reaction. Waves *A* and *C* being considered together, these are taken to represent two successive one-electron additions, of which the first is complete up to pH 9 and shows evidence of reversibility. It is suggested that the product of this reaction is a free radical such as (I) or (II). (Ionic dissociation is disregarded here.)



(I.)



(II.)



(III.)

The second reaction, which begins to decrease at about pH 5 and ceases at pH 8 (disappearance of wave *C*), is attributed to the reduction of (I) or (II) to dihydroquinaldinic acid. By analogy with the work of Levchenko (*loc. cit.*), Meisenheimer and Stotz (*Ber.*, 1925, **58**, 2330), and Knowles and Watt (*J. Amer. Chem. Soc.*, 1943, **65**, 410), the 1 : 4-isomer is the expected product. This reaction may be partly inhibited by the union of two free

radicals to yield a dimer of type (III). Coincident with the first decrease in the height of wave *A*, the badly-defined wave *D* appears, increasing in height as wave *C* becomes smaller. This indicates a third reaction, alternative to the second one, which is favoured by increase in pH. The effect of pH on wave *D* with respect to $E_{\frac{1}{2}}$ is quite different from that on waves *A* and *C* (Fig. 2). With the last two waves, $E_{\frac{1}{2}}$ is displaced to more negative potentials with increase in pH; with wave *D*, the small displacement observed is in the opposite direction. This indicates that hydrogen ions take part in the potential-determining reactions indicated by waves *A* and *C*, but that electron-capture is the primary process associated with wave *D*, followed by abstraction of a proton from the solvent as a non-potential-determining reaction.

Coincident with the second decrease in the height of wave *A* beyond pH 9, wave *E* rapidly increases in height up to pH 10·5, whereupon the rate of increase becomes small. As in the case of wave *A* at its greatest height, wave *E* corresponds with a two-electron reduction. Since the effect of pH on $E_{\frac{1}{2}}$ is similar to that observed in the case of wave *D*, the general nature of the reaction is also one of electron-capture. Logarithmic analysis of wave *E* at pH 10·7 yields a linear curve, the reciprocal slope of which is 0·089. The theoretical value for a reversible two-electron reaction is 0·030, and for a reversible one-electron reaction, 0·059. Hence it is concluded that reduction in alkaline solution affords no evidence of reversibility.

Only the major waves *A* and *E* being considered, the system of two waves of equal maximum height, one preponderating in acid, the other in alkaline solutions, resembles that observed in the polarography of substances capable of existence in two forms, *e.g.*, tautomers (cf. Müller and Baumberger, *J. Amer. Chem. Soc.*, 1939, **61**, 590; Langer, *Ind. Eng. Chem. Anal.*, 1942, **14**, 283). It is hoped when conditions permit to examine the reduction on a larger scale by the controlled potential method developed by Lingane, Swain, and Fields (*J. Amer. Chem. Soc.*, 1943, **65**, 1348), for isolation of the products should throw more light on the reaction mechanism. Until then, the author adopts Tachi and Kabai's suggestion (*loc. cit.*) that the " dissociated " (quinolinium) molecules are more readily reduced than those existing in the " undissociated " (quinolinium hydroxide) form.

The small wave *B* occurring in strongly acid solutions is taken to indicate some formation of tetrahydroquinaldinic acid (Wieland, Hettche, and Hoshino, *Ber.*, 1928, **61**, 2377). Since wave *A* does not attain its maximum height until pH 3, when wave *B* has become very small, the formation of the tetrahydro-derivative occurs directly without proceeding through the dihydro-stage.

Experimental.

Quinaldinic Acid.—The B.D.H. anhydrous product was recrystallised from benzene and dried at 105°; m.p. 157° (corr.). A 0·025M-stock solution in 50% aldehyde-free alcohol was prepared and diluted 25 times or as required with the appropriate buffer. The introduction of these small concentrations of alcohol was found to be without measurable effect upon the pH. Aqueous solutions made by neutralising the acid with sodium hydroxide grew moulds.

Buffer Solutions.—These were prepared from " AnalaR " reagents and examined polarographically for reducible impurities. Solutions of pH 5·8 and below were sulphuric acid–acetate mixtures 0·2M in sodium acetate, and Clark and Lubs's phosphate and borate buffers were used over the remainder of the range.

Apparatus.—Manual apparatus similar to that described by Kolthoff and Lingane (*op. cit.*, p. 215) was used. A saturated calomel half cell with an electrode area of 16 cm.^{2} served as external anode, being connected to the test solution by means of a salt bridge. Dissolved oxygen was removed from the solution by a stream of purified nitrogen which was first passed through a bubbler containing a little of the solution under examination. Bubbler, electrolysis cell, and calomel half cell were all maintained at 25·0°$\pm$0·2° in a large thermostat. The characteristics of the dropping electrode were: $m = 0{\cdot}917$ mg. sec.$^{-1}$, $t = 3{\cdot}39$ secs., $m^{2/3}t^{1/6} = 1{\cdot}157$ (determined in 0·1M-potassium chloride solution at 25°). Applied voltage was measured by means of a " Granta Minor " potentiometer, and was corrected for the IR drop due to the resistance of the cell. The current was measured by a calibrated Tinsley galvanometer with enclosed lamp and scale. The pH of the solutions was determined at 25° by the hydrogen electrode, values below 8 being checked by the quinhydrone electrode.

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117. *Reduction by Dissolving Metals. Part I.*

By Arthur J. Birch.

Sodium in liquid ammonia in presence or absence of available hydrogen from alcohols shows very different reducing properties. The former combination is capable of reducing sodium α- and β-naphthoxides and a number of methoxyalkylbenzenes and alkylbenzenes to the αδ-dihydro-derivatives shown in Tables I, II, and III. It appears to be anionoid in character, and rules governing the effect of methoxy-groups, alkyl groups, and saturated rings on the positions of reduction are given.

In many cases of reduction by dissolving metals it is clear that the initial stage consists of electron addition; in other cases " nascent " (possibly atomic) hydrogen may be added directly (cf. Campbell and Campbell, *Chem. Rev.*, 1942, **31**, 78). Since sodium in liquid ammonia behaves as a solution of metal kations and solvated electrons in equilibrium with metal atoms (Kraus, *J. Amer. Chem. Soc.*, 1921, **43**, 764), it might be expected to reduce by " electron addition," but the addition of a ready proton source, such as an alcohol, to the reagent renders reduction by " nascent " hydrogen a possibility. The action of sodium in liquid ammonia on a number of naphthalene and benzene derivatives in presence and in absence of an alcohol has now been examined in order to determine whether the presence of the latter alters the course of the reaction.

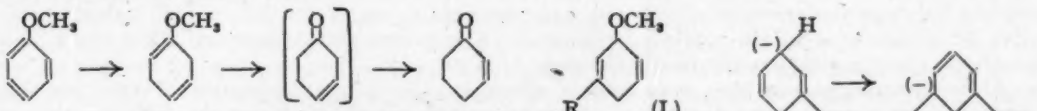
Preliminary experiments on sodium α- and β-naphthoxides (Table I) definitely indicated that a considerable change was produced by addition of *tert.*-amyl alcohol (chosen as a proton source unlikely to displace any of the phenol from its sodium salt), since sodium alone produced little reduction, but in presence of the alcohol good yields of dihydro-derivatives were obtained. Sodium α-naphthoate, however, was reduced readily in absence of alcohol, probably because the carboxyl ion is capable of taking up electrons by an electromeric mechanism, despite its negative charge. As a preparative method for 5 : 8-dihydro-α-naphthol and β-tetralone it is not necessary to employ the sodium salt, the free phenol acting as a partial source of hydrogen for its own reduction.

TABLE I.

Substance reduced (2 atoms of sodium).	Product.
Sodium α-naphthoxide	5 : 8-Dihydro-α-naphthol (trace)
α-Naphthol and *tert.*-C_5H_{11}·OH (1 mol.)	5 : 8-Dihydro-α-naphthol (65%)
Sodium α-naphthoxide and *tert.*-C_5H_{11}·OH (2 mols.)	5 : 8-Dihydro-α-naphthol (85%)
Sodium β-naphthoxide	(? 5 : 8)-Dihydro-β-naphthol (trace) and β-tetralone (trace)
β-Naphthol and *tert.*-C_5H_{11}·OH (1 mol.)	β-Tetralone (65%)
Sodium β-naphthoxide and *tert.*-C_5H_{11}·OH (2 mols.)	β-Tetralone (55%)

Freudenberg, Lautsch, and Piazolo (*Ber.*, 1941, **74**, 1886) found that potassium in liquid ammonia acts on methoxybenzene derivatives merely as a demethylating agent, and this was found to be true also for sodium, no appreciable reduction occurring. Wooster (U.S.P., 1938, 2,182,242) reduced a number of compounds containing an isolated benzene ring, including anisole, by sodium and methyl alcohol in liquid ammonia, and concluded that dihydro-derivatives were formed, although this was proved definitely only for benzene itself. This work has been confirmed and extended by reduction of the methoxyalkyl- and alkyl-benzenes shown in Tables II and III, ethyl being substituted for methyl alcohol in some cases.

The methoxyalkylbenzenes gave about 10% of the phenol formed by demethylation, and a mixture of starting material and reduction product which was difficult to separate into its pure components owing to their similar physical properties. The presence of the dihydro-derivatives was proved by treatment with hot dilute mineral acid, the products being αβ-unsaturated ketones; 3-methylanisole, for instance, gave 3-methyl-Δ^3-*cyclo*hexenone. There is no doubt that the ketones are αβ-unsaturated from the agreement in properties between their derivatives and those of the latter, when known, and from the formation of semicarbazido-semicarbazones in a number of cases, but it is clear that the initial dihydro-derivatives do not contain the conjugated bonds this evidence may appear to indicate. This follows from the fact that such bond systems are reduced more readily than the benzene rings under the conditions used, and from the fact that the product from 3-methylanisole (3-*methyl*-2 : 5-*dihydroanisole*) shows no light absorption in the region 2400—2800 A. The course of the series of reactions is as follows :



$CH_2{:}C(CH_3){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2R'$.

(II.) $R' = C(CH_3){:}CH{\cdot}CH_2{\cdot}OCH_3$. (VI.) $R' = C(CH_3)(OH){\cdot}CH{:}CH_2$.
(III.) $R' = C(CH_3){:}CH{\cdot}CH_3$. (VII.) $R' = C(CH_3){:}CH{\cdot}CH_2OH$.

It is, in general, unlikely that any appreciable amount of a dihydro-derivative of type (I) is produced, since this would give a benzene, rather than a *cyclo*hexenone derivative by the action of acid, and would, in any case, lose the methoxyl by further reduction. This was shown by reducing geranyl methyl ether (II) to geraniolene (III) under the same conditions, although the methoxyl is activated by only one double bond. In the unique case of 3-methylanisole, the formation of a small proportion of hydrocarbon giving derivatives of 1-methyl-Δ^1-*cyclo*hexene can be explained by reduction of (I, R = CH_3). That the hydrocarbon is a tetrahydro-, rather than a dihydro-benzene seems to indicate the intermediate formation and further reduction of a conjugated diene, probably by way of the electromeric change (IV) ⟶ (V). A similar rearrangement of an anion must be postulated in the reduction by this process of linalol (VI) to give a hydrocarbon (III) identical with that obtained from geraniol (VII) (Chablay, *Ann. Chim.*, 1917, **8**, 192; Dupont, Dulou, and Desreux, *Bull. Soc. chim.*, 1939, **6**, 83).

The initial dihydro-derivatives were converted directly into the unsaturated ketones, and these estimated as derivatives, usually with semicarbazide, but in the cases of (A), (K), and (P) (see Table II) with 2 : 4-dinitrophenylhydrazine. The yields shown represent the proportion of ketone in the crude product, calculated on the derivative, and the product shown is the principal one; in the case of (B) some of the alternative αβ-unsaturated ketone (2-methyl-Δ^2-*cyclo*hexenone) was probably present.

On the reasonable assumption that the αβ-unsaturated ketones are formed from the βγ- by bond shift by the shortest route the positions of addition of the hydrogen atoms to the anisole are given in the last column.

Reduction of several benzenoid hydrocarbons under similar conditions gave the products shown in Table III.

Owing to the similarity in boiling point it was difficult to separate the dihydro-derivatives from starting material, but the product from *m*-xylene was shown to contain only about 21% of benzenoid material by means of its ultra-violet absorption spectrum. The transparency of the compound in the region 2300—2800 A.,

TABLE II.

Compound.	Product.	Yield, %.	Atoms of H per mol.	Positions of added H atoms.
A. Anisole	Δ^2-*cyclo*Hexenone	20	2·4 (EtOH)	2 : 5
B. 2-Methylanisole	6-Methyl-Δ^2-*cyclo*hexenone	12	2·4 (EtOH)	3 : 6
C. 3-Methylanisole	3-Methyl-Δ^2-*cyclo*hexenone	42	4·0 (EtOH)	2 : 5
D. 4-Methylanisole	4-Methyl-Δ^2-*cyclo*hexenone	33	4·0 (MeOH)	2 : 5
E. 2 : 6-Dimethylanisole	2 : 6-Dimethyl-Δ^2-*cyclo*-hexenone	10	2·4 (EtOH)	2 : 5
F. 2 : 5-Dimethylanisole	(? 3 : 6)-Dimethyl-Δ^2-*cyclo*-hexenone	15	2·4 (EtOH)	3 : 6?
G. 2 : 4-Dimethylanisole	4 : 6-Dimethyl-Δ^2-*cyclo*-hexenone	22	2·4 (MeOH)	3 : 6
H. 3 : 4-Dimethylanisole	(? 3 : 4)-Dimethyl-Δ^2-*cyclo*-hexenone	35	2·4 (MeOH)	2 · 5?
J. 3 : 5-Dimethylanisole	3 : 5-Dimethyl-Δ^2-*cyclo*-hexenone	16	4·0 (EtOH)	2 : 5
K. 5-Methoxy-1 : 2 : 3 : 4-tetrahydronaphthalene	1-Keto-$\Delta^{9:10}$-octalin	trace	8·0 (EtOH)	7 : 10
L. 6-Methoxy-1 : 2 : 3 : 4-tetrahydronaphthalene	2-Keto-$\Delta^{7:9}$-octalin	44	2·5 (MeOH)	5 : 8
M. 6-Methoxy-5-methyl-1 : 2 : 3 : 4-tetrahydro-naphthalene	No ketonic product			
N. 5-Methoxyhydrindene	5-Keto-$\Delta^{6:9}$-tetrahydro-hydrindene	30	4·0 (EtOH)	4 : 8
P. 5-Methyl-2-*iso*propylanisole	3-Methyl-6-*iso*propyl-Δ^2-*cyclo*-hexenone (piperitone)	small	4·0 (MeOH)	3 : 6

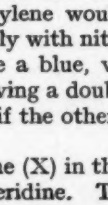
TABLE III.

Compound.	Product.
Q. 1 : 2 : 3 : 4-Tetrahydronaphthalene	1 : 2 : 3 : 4 : 5 : 8-Hexahydronaphthalene (IX)
R. *m*-Xylene	2 : 5-Dihydro-*m*-xylene (VIII)
S. *p*-Xylene	(? 2 : 5)-Dihydro-*p*-xylene
T. *p*-Cymene	γ-Terpinene (X)

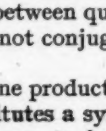
except for bands definitely due to *m*-xylene, demonstrates the absence of a conjugated bond system. The constitution was proved to be (VIII) by ozonolysis, a considerable proportion of acetylacetone being isolated from the product as its copper salt. The hydrocarbon also gave a crystalline *nitrosochloride* and *nitrolpiperidine*. Removal of hydrogen chloride from the former by means of aqueous-alcoholic sodium hydroxide gave 2 : 4 : 2′ : 4′-tetramethylazoxybenzene, doubtless by way of the phenylhydroxylamine (cf. Richter and Wolff, *Ber.*, 1930, **63**, 1714). This confirms the structure, since it locates the nitroso-group in the nitrosochloride on C_4 and therefore indicates the presence of a double bond between C_3 and C_4 in the original hydrocarbon. The alternative 1 : 4-dihydro-*m*-xylene would give 2 : 6 : 2′ : 6′-tetramethylazoxybenzene, since the 2 : 3-double bond would react preferentially with nitrosyl chloride.

The reduced tetralin gave a blue, very soluble *nitrosochloride*. Since derivatives of this type are only produced from substances having a double bond between quaternary carbon atoms, this indicates the presence of a 9 : 10-double bond, and if the other bond is not conjugated, as seems very likely, the constitution of the hydrocarbon must be (IX).

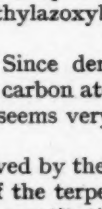
The presence of γ-terpinene (X) in the *p*-cymene product was proved by the formation of the characteristic nitrosochloride and nitrolpiperidine. This constitutes a synthesis of the terpene. The ready formation of a *nitrosochloride* from the *p*-xylene compound appears to favour the constitution given, which would also be expected by analogy with *p*-cymene.



(VIII.)



(IX.)

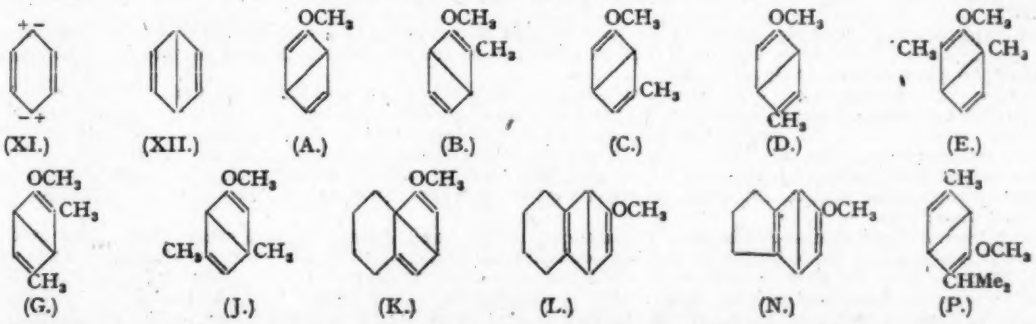


(X.)

It is clear that electron addition must be an anionoid process, and this appears to be the case with the nascent hydrogen reduction also, since the sodium phenoxides are not reduced—the naphthoxides are so probably by virtue of the greater polarisability of the naphthalene ring—and there is no evidence of reduction being initiated in the position occupied by, or para to the methoxyl group, with the minor exception of (C). Sachs (*Ber.*, 1906, **39**, 3006) found that sodamide, a typically anionoid reagent, reacts with sodium α- and β-naphthoxide to give sodium 5-amino-α- and -β-naphthoxide, thus leading to the expectation that an anionoid reduction should take place in the unsubstituted ring in both cases. This is not fulfilled for sodium β-naphthoxide, which is probably first reduced to sodium 1 : 4-dihydro-β-naphthoxide, and the reagent appears to be kationoid. Since free radicals behave amphoterically according to the type of activation in the substrate molecule (Hey and Waters, *Chem. Rev.*, 1937, **21**, 187), the intervention of hydrogen atoms may explain this result, the anionoid activation of the 1-position of sodium β-naphthoxide being particularly high.

On the assumption of anionoid reduction it should be possible to correlate the orientation influences of methoxyl and alkyl groups with those observed for other anionoid reagents. Data are scarce, but Sartoretto

and Sowa (*J. Amer. Chem. Soc.*, 1937, **59**, 603), by a comparison of the effect of substituents on the direction of cleavage of diphenyl ethers by sodium in liquid ammonia, showed that deactivation (increasing order of intensity) was produced by *o*-CH_3, *p*-CH_3, and *p*-OCH_3, and activation by *o*-OCH_3. Since the reductions are $\alpha\delta$, the benzene ring must tend to polarise for reaction as in (XI), initial addition occurring at the positive pole; for convenience these activated forms may be written as the Dewar formula (XII). It is evident from the results of Sartoretto and Sowa, and from the known inductive effect of alkyl groups, that these will tend to prevent addition of an anionoid reagent in the substituted position, or para to it, so that the bridge of the Dewar formula corresponding to the principal reduction product will end on the least number of alkyl groups. This is obviously true for the hydrocarbons (Q), (R), and (T) (Table III). In the methoxyalkylbenzene series no reduction is initiated in the position occupied by, or para to a methoxyl except to a small extent with (C), and the rule can therefore be extended to cover these compounds by omitting from consideration the Dewar formula having a methoxyl at the bridge head. This result, which also agrees with those of Sartoretto and Sowa, shows that the unshared electrons of the oxygen atom must strongly repress reaction of both the occupied and the para-position towards an anionoid reagent, and oppose the inductive effect of the methoxyl which would be expected to assist the process. The rule may be stated so as to cover all the cases as follows. If a benzene ring bearing methoxyl and alkyl groups (or the ends of a saturated ring) is written in the Dewar formulæ in which the bridge head is not occupied by a methoxyl group, the chief reduction product will correspond to the formula having the least number of substituents at the bridge heads. The formulæ corresponding to the products definitely identified in Table II are given below, and the rule is easily verified.



2 : 3-Disubstituted anisoles, such as (K), give two possible formulæ between which the rule does not distinguish, and it is necessary to restate it somewhat differently. Reduction will tend to be initiated (*a*) in an unoccupied position and (*b*) *o*- or *m*- rather than *p*- to an alkyl or methoxyl group, the latter having the greater deactivating effect in both cases. With (K) it is impossible for both these rules to be obeyed, and from the nature of the product (*a*) or (*b*) must have preponderance according to whether reduction is initiated *m*- or *o*- to the methoxyl group. The latter is the more probable position from the results of Sartoretto and Sowa (*loc. cit.*), but since the addendum is symmetrical it is impossible to decide at present.

The mechanism of the " nascent hydrogen " reduction is still in doubt. It must differ from that of " electron addition " in which bivalent anions are produced from polycyclic compounds as the initial stage (Hückel and Bretschneider, *Annalen*, 1939, **540**, 157; Wawzonek and Laitinen, *J. Amer. Chem. Soc.*, 1942, **64**, 2365), evidently because the greater resonance in an isolated benzene ring renders the production of such anions difficult. It is also evident that univalent anions such as (IV) cannot be intermediates, since, as already seen, these would give tetrahydro- rather than dihydro-derivatives. It is possible that in presence of available protons the formation of a charged ring is avoided. An alternative hypothesis is that reduction is due to hydrogen atoms, since Geib and Harteck (*Ber.*, 1933, **66**, 1815) have shown that these, in the gaseous state, are capable of reducing benzene. Metallic iron catalyses the combination of hydrogen atoms to molecules, and it was found that 6-methoxytetralin (L) and sodium β-naphthoxide were not reduced in presence of a little of the finely divided metal. This may be due merely to removal of the sodium by reaction with ammonia, also catalysed by iron, but this process also produces " nascent " hydrogen, so the state of the latter must be important.

The practical application of this type of reduction is limited by the low solubility of many compounds in liquid ammonia, since reduction is in competition with hydrogen evolution.

Experimental.

Naphthalene Derivatives.—The apparatus and conditions used in the following experiments were the same, the anhydrous liquid ammonia being drawn from a cylinder into a 350-c.c. Dewar flask, and the reaction carried out with stirring.

Reduction of α-naphthol. (i) α-Naphthol (5·5 g.) was treated with finely powdered sodamide (1·5 g.) in liquid ammonia (60 c.c.), and sodium (1·8 g.) added in small pieces during an hour. When the blue colour had disappeared, the ammonia was evaporated, and the residue decomposed with ice and dilute hydrochloric acid. Extraction of the product with ether and fractionation from benzene–light petroleum showed it to consist mainly of starting material, m. p. 94°, but the more soluble fraction, after removal of the naphthol as its picrate by treatment with alcoholic picric acid, gave 5 : 8-dihydro-α-naphthol (0·3 g.) as colourless prisms, m. p. and mixed m. p. 74° (Rowe and Levin, J., 1921, **119**, 2023, give m. p. 75°).

(ii) As above, but the sodamide being omitted and *tert.*-amyl alcohol added (2·9 g.) with the naphthol. The 5 : 8-dihydro-α-naphthol crystallised from benzene–light petroleum as massive colourless prisms (3·2 g.), m. p. and mixed m. p. 74°. This method of preparation is superior to that of Rowe and Levin (*loc. cit.*).

(iii) To α-naphthol (10 g.) and powdered sodamide (2·7 g.) in ammonia (100 c.c.) was added *tert.*-amyl alcohol (12·5 g.) and then sodium (3·2 g.) in small pieces. Most of the ammonia was evaporated, water (100 c.c.) added, and the solution extracted several times with ether. It was then acidified, and the precipitated oil, which rapidly solidified, recrystallised from light petroleum (b. p. 80—100°). 5 : 8-Dihydro-α-naphthol (8·5 g.) was obtained as massive colourless prisms, m. p. 71—74°, undepressed by an authentic specimen. A further 0·6 g. of less pure material was obtained from the mother-liquor.

Reduction of β-naphthol. (i) β-Naphthol (15 g.) and sodamide (4·0 g.) in liquid ammonia (140 c.c.) were treated with sodium (4·6 g.) in small pieces. After the blue colour had disappeared the ammonia was evaporated, and the residue decomposed with ice. This, like all alkaline solutions of the reduction products of β-naphthol, had to be protected as far as possible from the air, and worked up quickly to avoid the formation of tetralone-blue. Immediate extraction with ether gave only a trace of β-tetralone, but after acidification and exhaustion of the ethereal extract with 10% sodium hydroxide the ether contained 2·2 g. of neutral oil, which gave a crystalline derivative with sodium bisulphite. Decomposition of this with dilute sulphuric acid gave β-tetralone (1·2 g.), b. p. 140°/14 mm.; semicarbazone, m. p. and mixed m. p. with an authentic specimen kindly presented by Dr. J. W. Cornforth, 193°. The above alkaline solution was treated with methyl sulphate, and the resulting solid recrystallised from alcohol, giving 2-methoxynaphthalene (8 g.). The mother-liquor from the crystallisation was treated with alcoholic picric acid, the picrate removed, and the alcohol evaporated. The residual oil was taken up in ether, washed with 10% sodium hydroxide solution, dried, and distilled, yielding a colourless oil with a phenolic odour (0·9 g.), b. p. 145—150°/14 mm. It seemed to be mainly an *ar-dihydro-2-methoxynaphthalene* (Found: C, 82·0; H, 7·7. $C_{11}H_{12}O$ requires C, 82·5; H, 7·5%).

(ii) As above, but with *tert.*-amyl alcohol (8·5 g.) instead of sodamide. The neutral product (10·5 g.), b. p. 138—140°/14 mm., was purified through the bisulphite compound, giving β-tetralone (9·8 g.), b. p. 140°/13 mm.; semicarbazone, m. p. 193°.

(iii) β-Naphthol (5 g.) and sodamide (1·3 g.) were brought into reaction in liquid ammonia (50 c.c.), and *tert.*-amyl alcohol (5·6 g.) added, followed by sodium (1·5 g.) in small pieces, and the ketonic product worked up as above, giving β-tetralone (2·6 g.), semicarbazone, m. p. 193°.

Reduction of α-naphthoic acid. α-Naphthoic acid (4·4 g.), sodamide (1 g.), and liquid ammonia (25 c.c.) were treated with sodium (1·2 g.) in small pieces, reaction being rapid. A small portion of the acid product recrystallised from benzene as colourless prisms, m. p. 75°, undepressed by an authentic sample of 1 : 4-dihydro-α-naphthoic acid prepared by Sowinski's method (*Ber.*, 1891, **24**, 2355). The remainder of the product was heated on the steam-bath for 30 mins. with an excess of 20% sodium hydroxide solution, and then acidified with dilute sulphuric acid. The product crystallised from aqueous acetic acid as colourless prisms (2·8 g.), m. p. 112°. Sowinski (*loc. cit.*) gives m. p. 112° for 3 : 4-dihydro-α-naphthoic acid.

Methoxybenzene Derivatives.—Materials. The anisole, *o*-, *m*-, and *p*-tolyl methyl ethers were from stock, the 5-methoxyhydrindene was made by the method of Cook and Linstead (J., 1934, 952), and 5-methoxy-1 : 2 : 3 : 4-tetrahydronaphthalene from the phenol obtained by reduction of α-naphthol in presence of Raney nickel at 125°/100 atm. The dimethylanisoles were obtained by methylation of the phenols: 3 : 4- from "1 : 2 : 4-xylenol," m. p. 61° (Kahlbaum); 2 : 5- from "*p*-xylenol," m. p. 74° (Schuchardt); 2 : 6- from "1 : 2 : 6-xylenol," m. p. 45—46° (I.C.I.); 2 : 4- from "1 : 3 : 4-xylenol," b. p. 210—212° (Kahlbaum); 3 : 5- from "1 : 3 : 5-xylenol," m. p. 65° (I.C.I.); and 5-methyl-2-*iso*propylanisole from thymol. 6-Methoxy-5-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene was kindly presented by Dr. R. H. Martin.

3-Methyl-2 : 5-dihydroanisole. A mixture of 3-methylanisole (20 g.) and methyl alcohol (28 g.) was dropped into a solution of sodium (20 g.) in liquid ammonia (500 c.c.) with stirring during an hour. The mixture was cautiously decomposed with ice and then with water, the organic layer collected with ether, and fractionated into two portions: (I) b. p. 105—120° (2·5 g.), (II) b. p. 165—173° (9·8 g.). Redistillation gave the fractions (A) b. p. 108—115° (2 g.), (B) b. p. 170—171° (9 g.). Fraction (A) gave a nitrosochloride, m. p. 92—93° (Found: C, 52·6; H, 7·6. Calc. for $C_7H_{12}ONCl$: C, 52·0; H, 7·4%), undepressed by an authentic sample of 1-methyl-Δ^1-*cyclo*hexene nitrosochloride, and it gave a nitrolpiperidine, m. p. 146—147°, undepressed by an authentic specimen of 1-methyl-Δ^1-*cyclo*hexene nitrolpiperidine, m. p. 146—147°.

Fraction (B) consisted essentially of *3-methyl-2 : 5-dihydroanisole* (Found: C, 77·2; H, 9·4. $C_8H_{12}O$ requires C, 77·4; H, 9·7%). The ultra-violet absorption spectrum showed no appreciable band in the region of 2400—2800 A., where conjugated double bonds would be expected to absorb, except a band at $\lambda_{max.}$ 2740 A.; $\epsilon_{max.}$ 410, corresponding to about 20% of starting material. An end absorption rising to $\epsilon = 3100$ at λ 2300 A. probably corresponds to the absorption of the enol ether double bond. (Measurements by Dr. F. B. Strauss, Oxford.)

A small portion of the fraction was refluxed with 10% aqueous sulphuric acid for an hour, the oil collected in ether, and heated on the steam-bath with excess of aqueous-alcoholic semicarbazide acetate. After addition of a little petrol, the solid was removed and extracted several times with small portions of boiling alcohol, leaving a white residue (*A*). Addition of a little water to the alcoholic extract gave colourless prisms (*B*). Fraction (*A*) recrystallised from a large volume of water as colourless needles, m. p. 210° (decomp.) (Found: C, 44·2; H, 7·3. $C_9H_{18}O_2N_6$ requires C, 43·7; H, 7·65%), apparently *3-methyl-*Δ^2-cyclo*hexenonesemicarbazido-semicarbazone*. Fraction (*B*) recrystallised from a little alcohol as flat colourless prisms, m. p. 199—200°. Vorländer and Gärtner (*Annalen*, 1899, **304**, 23) give m. p. 199—201° for the semicarbazone of 3-methyl-Δ^2-*cyclo*hexenone. Treatment of the semicarbazone with alcoholic 2 : 4-dinitrophenylhydrazine sulphate in alcohol gave the *2 : 4-dinitrophenylhydrazone* as dark red plates (from benzene–alcohol), m. p. 173° (Found: C, 53·4; H, 4·7. $C_{13}H_{14}O_4N_4$ requires C, 53·7; H, 4·8%).

If in the above reduction of 3-methylanisole the methyl alcohol was omitted, the disappearance of the sodium was slow, and about half the material was converted into the water-soluble sodium salt of *m*-cresol, identified by formation of the *m*-tolyloxyacetic acid, m. p. 102°, by treatment with sodium chloroacetate. The water-insoluble portion was nearly pure starting material, and after refluxing with dilute acid gave no derivative with 2 : 4-dinitrophenylhydrazine sulphate.

Reductions shown in Table II.—All the reductions were carried out in a similar manner in a 350-c.c. Dewar flask without external cooling. Continuous stirring was necessary, the mixture assuming a very pasty consistency towards the end. The example given below is typical, except that ether was added only in the cases of the methoxytetralins and methoxyhydrindene.

2-Keto-$\Delta^{1:9}$*-octalin.* 6-Methoxy-1 : 2 : 3 : 4-tetrahydronaphthalene (8·1 g.) and methyl alcohol (4 g.) were added to liquid ammonia (100 c.c.) and ether (30 c.c.), and sodium (3 g.) slowly added in pieces of about 0·2 g., the colour being allowed to disappear between additions. The ammonia was then mostly evaporated, the residue decomposed with ice and water, and the organic layer removed. Distillation gave a homogeneous fraction with practically the same b. p. as the starting material (235°) (6·8 g.). This was then refluxed with 10% sulphuric acid for an hour, extracted with ether, washed with sodium carbonate solution, the solvent evaporated, and the residual pleasant-smelling oil heated on

the steam-bath for 30 minutes with an excess of aqueous-alcoholic semicarbazide acetate. After cooling, light petroleum (25 c.c.) was added, the solid filtered off, washed with petrol and a little alcohol and then water, and dried (3·85 g.). It was practically pure 2-keto-$\Delta^{1:9}$-octalin semicarbazone; a little was recrystallised from dioxan–alcohol, being obtained as cream-coloured prisms, m. p. and mixed m. p. with an authentic specimen obtained by the method of du Feu, McQuillin, and Robinson (J., 1937, 53), 215°. The ketone was also characterised by addition of methylmagnesium iodide in the presence of cuprous bromide (Birch and Robinson, J., 1943, 501), the semicarbazone of *cis*-2-keto-9-methyldecalin being obtained from the product, m. p. and mixed m. p. 212—213°.

If the ammonia contained finely divided iron (1% by weight of the phenol ether) produced by the reduction of ferric nitrate by sodium, *in situ*, no ketonic product could be isolated, the substance being unchanged apart from a little demethylation.

The following substances were obtained from the other phenol ethers shown in Table II.

(A) *cyclo*Hexenone-2 : 4-dinitrophenylhydrazone as orange, flat needles from benzene–alcohol, m. p. 163°, undepressed by an authentic specimen.

(B) The semicarbazone of the product, crystallised from alcohol, had m. p. 164—165° (Found : C, 57·3; H, 7·8. Calc. for $C_9H_{13}ON_3$: C, 57·5; H, 7·8%). Kötz and Steinhorst (*Annalen*, 1911, **379**, 17) give m. p. 177—178° for the semicarbazone of 6-methyl-Δ^2-*cyclo*hexenone, and Wallach (*Annalen*, 1908, **369**, 303) m. p. 207—208° for that of the alternative 2-methyl-Δ^2-*cyclo*hexenone. Repeated crystallisation from methyl alcohol of the product from (B) slowly raised the m. p. to about 170°, and it appears to be derived mainly from the 6-methyl compound, since admixture with the 2-methyl derivative produced a depression in m. p. The original ketone gave a 2 : 4-*dinitrophenylhydrazone* as bright orange needles from benzene–alcohol, m. p. 122—126° (Found : C, 52·6; H, 4·75. $C_{15}H_{14}O_4N_4$ requires C, 53·7; H, 4·8%).

(D) 4-Methyl-Δ^2-*cyclo*hexenonesemicarbazone was obtained as colourless prisms from alcohol, m. p. 188—189° (Found : C, 57·2; H, 7·95. Calc. for $C_9H_{13}ON_3$: C, 57·5; H, 7·8%) : Kötz and Steinhorst (*loc. cit.*) give m. p. 184—185°. The ketone also gave a derivative with 2 : 4-dinitrophenylhydrazine as bright red prisms from benzene–alcohol, m. p. 158—159°.

(E) 2 : 6-*Dimethyl*-Δ^2-cyclo*hexenonesemicarbazone* was obtained as cream-coloured prisms from alcohol–dioxan, m. p. 210—211° (Found : C, 59·7; H, 8·5. $C_9H_{15}ON_3$ requires C, 59·7; H, 8·3%). The 2 : 4-dinitrophenylhydrazone consisted of flat, red needles (benzene–alcohol), m. p. 153°.

(F) 3 : 6(?)-*Dimethyl*-Δ^2-cyclo*hexenonesemicarbazido-semicarbazone* unaccompanied by any semicarbazone was obtained as small, colourless needles from a large volume of water, m. p. 214° (decomp.) (Found : C, 46·6; H, 7·9. $C_{12}H_{20}O_2N_6$ requires C, 46·9; H, 7·8%). The 2 : 4-*dinitrophenylhydrazone* crystallised from benzene–alcohol as orange-red needles, m. p. 134° (Found : C, 55·2; H, 5·3. $C_{14}H_{16}O_4N_4$ requires C, 55·3; H, 5·3%).

(G) 4 : 6-*Dimethyl*-Δ^2-cyclo*hexenonesemicarbazone* was obtained as cream-coloured prisms from alcohol, m. p. 175° (Found : C, 59·2; H, 8·2. $C_9H_{15}ON_3$ requires C, 59·7; H, 8·3%). Wallach (*Annalen*, 1913, **397**, 198) gives m. p. 194—195° for the alternative 2 : 4-dimethyl derivative. The 2 : 4-dinitrophenylhydrazone crystallised as flat, red needles from benzene–alcohol, m. p. 152°.

(H) 3 : 4-*Dimethyl*-Δ^2-cyclo*hexenone* (?) *semicarbazone* was obtained as cream-coloured prisms from alcohol, m. p. 193° (Found : C, 60·0; H, 8·5. $C_9H_{15}ON_3$ requires C, 59·7; H, 8·3%). The 2 : 4-dinitrophenylhydrazone crystallised from benzene–alcohol as red prisms, m. p. 146°.

(J) 3 : 5-Dimethyl-Δ^2-*cyclo*hexenonesemicarbazone was obtained as colourless prisms from alcohol, m. p. 177° (Found : C, 59·3; H, 8·65. Calc. for $C_9H_{15}ON_3$: C, 59·7; H, 8·3%) : Knoevenagel (*Annalen*, 1897, **297**, 165) gives m. p. 179—180°. A small amount of white, insoluble material, m. p. 199° (decomp.), which accompanied the semicarbazone is probably the semicarbazido-semicarbazone.

(K) The 2 : 4-dinitrophenylhydrazone was obtained as dark red, flat needles, m. p. 263° (decomp.), undepressed by an authentic specimen of 1-keto-$\Delta^{9:10}$-octalin-2 : 4-dinitrophenylhydrazone, m. p. 264°, derived from the ketone prepared in poor yield by oxidation of $\Delta^{9:10}$-octalin with selenium dioxide. Cook and Lawrence (J., 1937, 817) give m. p. 266·5—267° (decomp.).

(N) 5-*Keto*-$\Delta^{4:9}$-*tetrahydrohydrindenesemicarbazone* was obtained as cream-coloured prisms from dioxan–alcohol, m. p. 228—230° (Found : C, 61·9; H, 7·6. $C_{10}H_{15}ON_3$ requires C, 62·15; H, 7·8%). The 2 : 4-*dinitrophenylhydrazone* crystallised as red plates from dioxan–alcohol, m. p. 197—198° (Found : C, 57·2; H, 5·15. $C_{15}H_{16}O_4N_4$ requires C, 57·0; H, 5·1%).

For comparison, these substances were synthesised as follows. 2-Diethylaminomethyl*cyclo*pentanone (10 g.) and methyl iodide (10 g.) were mixed in ether (20 c.c.) and left overnight in the refrigerator. The ether was then decanted, the residual quaternary salt dissolved in alcohol and added to a cold solution of acetoacetic ester (15 g.) and sodium (3·2 g.) in alcohol (30 c.c.). After 3 hours it was heated on the steam-bath for a few minutes. Worked up in the usual manner, the product was a colourless, pleasant-smelling oil, b. p. 125°/10 mm. (3 g.), which gave derivatives shown to be identical with those above by mixed m. p.

(P) *dl*-Piperitone-2 : 4-dinitrophenylhydrazone was obtained from alcohol as orange needles, m. p. 117—118°, undepressed by an authentic specimen kindly supplied by Professor John Read, F.R.S.

Reduction of Geranyl Methyl Ether.—Geranyl methyl ether (b. p. 205—207°, 5 g.) and ethyl alcohol (6 g.) were added to liquid ammonia (40 c.c.), followed by sodium (3 g.) in small pieces over 45 minutes. Worked up as usual, the product was a colourless oil, b. p. 165—170° (Found : C, 86·7; H, 12·7. Calc. for $C_{10}H_{18}$: C, 87·0; H, 13·0%).

Absence of Compounds of Type (I).—In the cases of (B), (C), and (D), after removal of the semicarbazone the residue was distilled, and refluxed with a mixture of equal volumes of hydrobromic acid (*d* 1·5) and acetic acid for an hour. In all cases the product was almost completely soluble in dilute sodium hydroxide solution.

Alkylbenzenes.—The reductions were carried out in a similar manner to that used by Wooster (*loc. cit.*), except that no external cooling was used. The sodium was dissolved in liquid ammonia in a Dewar flask, and a mixture of the hydrocarbon and ethyl alcohol equivalent to the sodium used was slowly dropped in with stirring.

Reduction of m-*xylene.* Hydrocarbon (18 g.) and alcohol (25 c.c.) were added to a solution of sodium (10 g.) in liquid ammonia (150 c.c.). The product was a colourless oil, b. p. 142—144° (15 g.) (Found : C, 89·1; H, 10·8. C_8H_{12} requires C, 88·9; H, 11·1%). It gave the following absorption bands corresponding to *m*-xylene, the proportion of the latter being calculated from the values of ϵ given for the pure substance by Wolf and Herold (*Z. physikal. Chem.*, 1931, *B*, **13**, 213) (data by Dr. F. B. Strauss, Oxford) :

$\gamma_{max.}$, A.	<2290	2657	2687	2726
$\epsilon_{max.}$	—	59·4	41·1	54·8
m-Xylene, %	—	21·6	18·0	21·8

Treatment with amyl nitrite and hydrochloric acid in acetic acid in the usual manner (Wallach, *Annalen*, 1906, **343**, 49) gave the *nitrosochloride* as colourless needles, m. p. 123° (decomp.) (Found : C, 55·8; H, 7·1. $C_9H_{13}ONCl$ requires C, 55·3; H, 6·9%). This on heating with a few drops of piperidine in alcohol gave the *nitrolpiperidine* as prismatic needles, m. p. 137° (Found : C, 70·1; H, 9·3. $C_{13}H_{22}ON_2$ requires C, 70·3; H, 9·0%).

The nitrosochloride (1 g.) was heated on the steam-bath for 15 minutes with 10 c.c. of a mixture of equal volumes of alcohol and 20% aqueous sodium hydroxide, and the mixture then added to 30% aqueous sulphuric acid (10 c.c.). The solid precipitate was recrystallised first from a little alcohol and then from a little light petroleum (b. p. 40—60°). It consisted of pale yellow prisms, m. p. 75° (Found: C, 75·3; H, 7·3. Calc. for $C_{16}H_{18}ON_2$: C, 75·6; H, 7·1%). Bamberger and Brady (*Ber.*, 1900, **33**, 3644) give m. p. 76—76·5° for 2 : 2′ : 4 : 4′-tetramethylazoxybenzene, and Bamberger and Rising (*Annalen*, 1901, **316**, 265) give m. p. 88·5—89° for the alternative 2 : 2′ : 6 : 6′-tetramethylazoxybenzene.

Reduced hydrocarbon (3·2 g.) in chloroform (25 c.c.) was ozonised, the ozonide being decomposed with water and zinc dust. The chloroform solution was filtered, and well shaken with a solution of copper acetate (10 g.) in warm water (100 c.c.). The chloroform layer was separated, dried, and evaporated, leaving a copper compound which recrystallised from chloroform–ether as blue needles (0·7 g.); this did not melt below 300° (Found: C, 45·6; H, 5·5. Calc. for $C_{16}H_{14}O_4Cu$: C, 45·8; H, 5·3%). It was, therefore, the copper salt of acetylacetone.

Reduction of tetralin. Addition of tetralin (13·2 g.) and ethyl alcohol (18 g.) to a solution of sodium (9·2 g.) in liquid ammonia (250 c.c.) gave a colourless oil (12 g.), b. p. 204—208°. Treatment with amyl nitrite and hydrochloric acid in acetic acid solution gave a bright blue colour, but no precipitate. After evaporation at room temperature in a vacuum a blue solid was obtained, which recrystallised from a little light petroleum as bright blue prisms, resembling copper sulphate, m. p. 91° (Found: C, 59·9; H, 7·1. $C_{10}H_{14}ONCl$ requires C, 60·0; H, 7·0%), doubtless the *nitrosochloride* of 1 : 2 : 3 : 4 : 5 : 8-hexahydronaphthalene.

Reduction of p-*cymene.* *p*-Cymene (10 g.) and alcohol (20 g.) were added to sodium (10 g.) in liquid ammonia (200 c.c.). The product (9·5 g.) was a colourless oil with a slight lemon odour, b. p. 175—180° (1 G. absorbed 98 c.c. of hydrogen in the presence of Raney nickel, corresponding to 15% of substance with two double bonds). Fractionation gave a fraction, b. p. 179—180° (Found: C, 89·2; H, 11·0. Calc. for $C_{10}H_{14}$: C, 89·6; H, 10·4%. Calc. for $C_{10}H_{16}$: C, 88·2; H, 11·8%). From the analysis this fraction contained about 25—30% of a dihydro-*p*-cymene, consisting at least partly of γ-terpinene, since the nitrosochloride, m. p. 110°, and nitrolpiperidine, m. p. and mixed m. p. with an authentic specimen 144°, were obtained from it.

Reduction of p-*xylene.* *p*-Xylene (10·6 g.) was reduced with sodium (9·2 g.) and alcohol (24 c.c.) in ammonia (150 c.c.), giving a product (9 g.), b. p. 140—142°. This gave a nitrosochloride (2·2 g.) as colourless needles, m. p. 98°, a little of which was converted into the nitrolpiperidine, m. p. 133°. The nitrosochloride, after being heated with 20 c.c. of a mixture of equal volumes of alcohol and 20% sodium hydroxide on the steam-bath for 15 minutes, and then diluted with 20 c.c. of 30% sulphuric acid, gave a yellow solid which recrystallised as sulphur-yellow needles from methyl alcohol, m. p. 110° (Found: C, 75·3; H, 7·3. Calc. for $C_{16}H_{18}ON_2$: C, 75·6; H, 7·1%). Bamberger and Rising (*Annalen*, 1901, **316**, 290) give m. p. 110—110·5° for 2 : 2′ : 5 : 5′-tetramethylazoxybenzene.

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118. *The Kinetics of Anionotropic Rearrangement. Part I. The Rearrangement of Propenylethynylcarbinol.*

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A kinetic study of the acid-catalysed anionotropic rearrangement:

$$CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH \longrightarrow CH_3{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}C{\vdots}CH$$

has been made, the course of the reaction being followed by measuring the changing absorption of ultra-violet light. This accurate and convenient method of determining reaction rates is of wide applicability but has been little employed hitherto. In aqueous solution containing 20% by volume of alcohol the reaction is of the first order, the rate being independent of the initial concentration of the carbinol, strictly proportional to the hydrogen-ion concentration at low, and to Hammett's acidity function at high acidities, and almost identical with the rate of racemisation. The salt effect is positive. The experimental energy of activation varies from 19 to 24 kg.-cals. over a wide range of conditions. The mechanism of the reaction is discussed with reference to current theories of anionotropy, and the oxonium ion (II; see p. 443) is suggested as the principal intermediate.

ALTHOUGH tautomeric systems of the type $X{-}A{-}B{=}C \rightleftharpoons A{=}B{-}C{-}X$ (where X is an anion) have long been known, and have been recognised as counterparts to prototropic systems during the past twenty years, few quantitative kinetic studies of anionotropy have been made. The work of Burton and Ingold (J., 1928, 904) and of Burton (J., 1928, 1650 *et seq.*) on the rearrangement of arylallylcarbinols was entirely qualitative, and the velocity measurements reported by Kenyon, Partridge, and Phillips (J., 1937, 207) are rather incomplete. Meisenheimer and Beutter (*Annalen*, 1937, **508**, 58) made a quantitative study of the replacement acetylation of cinnamyl chloride, but not primarily from the point of view of the simultaneous partial rearrangement to the phenylallyl derivative. Similarly, the work of Meisenheimer and Link (*Annalen*, 1930, **479**, 211), and of Young and Lane (*J. Amer. Chem. Soc.*, 1938, **60**, 847) on replacement halogenations in the phenylvinylcarbinol and the crotyl alcohol series, was concerned mainly with the analysis of reaction products.

The range of examples of simple anionotropic systems has recently been considerably extended by the discovery (Jones and McCombie, J., 1943, 261 and subsequent papers) of rearrangements such as:

$$CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH \xrightarrow{\text{acid}} CH_3{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}C{\vdots}CH$$

which, in common with the cases cited above, involve the formation of a conjugated system, but have the advantage of being purely aliphatic in nature, thus avoiding complications arising from the presence of a benzenoid ring. A ready means of following the rate of rearrangements of this type is provided by the large difference in ultra-violet light absorption between isolated and conjugated vinylacetylene systems. For work in dilute solution, absorption spectrophotometric assay is far more convenient and accurate than, for instance,

the determination of refractive index or chemical analysis, which often involves the isolation of the reaction products at several stages of the reaction. The wide scope and great potentialities of this method of studying reaction kinetics deserve special emphasis. Visible and infra-red light absorption have been utilised for the determination of reaction rates in a limited number of cases, but ultra-violet light absorption, which is more widely applicable to organic systems than the former and more easily accessible experimentally at present than the latter, does not appear to have been used previously in this way except by Batley (*Trans. Faraday Soc.*, 1928, **24**, 438). With photographic spectrophotometry, the accuracy of the rate constants obtained by this method is limited to about 1%, as it is in most other methods commonly employed, but by the introduction of photoelectric spectrophotometry much higher precision could be attained. Actually, the limit to accuracy is generally set by internal factors such as the incomplete exclusion of side reactions.

The present paper deals exclusively with the rearrangement of propenylethynylcarbinol, but the kinetics of other cases of the anionotropic formation of vinylacetylene systems have been examined and will be reported in due course. The investigation will also be extended to embrace anionotropic changes yielding styrene, butadiene, and higher polyene and polyenyne systems.

The heterogeneous conditions of rearrangement used by Jones and McCombie (*loc. cit.*) were obviously unsuitable for kinetic studies, propenylethynylcarbinol and its isomer, hex-3-en-5-yn-2-ol, being only sparingly soluble in water. Although the use of an aqueous medium in the study of reactions involving ionic components has theoretical disadvantages (see Bell, *Trans. Faraday Soc.*, 1938, **34**, 234), the lack of knowledge regarding acid strengths in other solvents made it, nevertheless, desirable, in the first instance, to retain water as the principal component of the reaction medium. An organic solvent was sought which (i) is miscible with water and the carbinols, (ii) has low ultra-violet light absorption, (iii) is unaffected by acids over prolonged periods, and (iv) does not interact with propenylethynylcarbinol, its isomer, or any intermediates in the presence of acids. Alcohol was an obvious choice, after it had been ascertained that no ether formation took place in hydrochloric acid solutions containing up to 80% by volume of alcohol, other solvents such as acetone or dioxan, in which ether formation is impossible, being excluded because of conditions (ii) and (iii).

In a water–alcohol mixture containing 20% by volume of alcohol the reaction is strictly of the first order (see Experimental) and the rate constant is independent of the initial concentration of carbinol between $c = 0{\cdot}02$ and 0·15 mol./l. At higher concentrations, when the carbinol becomes an appreciable constituent of the reaction medium, a slight decrease in the rate constant occurs (Table I), similar in magnitude to that produced by increasing the alcohol concentration (unpublished observation). In the range of conditions investigated, the reaction product is always hex-3-en-5-yn-2-ol and the reaction goes to > 98% completion, as indicated by the final

TABLE I.

Reaction medium, 20% aqueous EtOH;* $t = 30{\cdot}0°$; k = first-order rate constant; c = concentration of carbinol.

c (g./100 ml.).	c (mols./l.).	$k \times 10^4$ (min.$^{-1}$).	c (g./100 ml.).	c (mols./l.).	$k \times 10^4$ (min.$^{-1}$).	c (g./100 ml.).	c (mols./l.).	$k \times 10^4$ (min.$^{-1}$).
Catalyst, 0·4M-HCl.						Catalyst, 2M-HCl.		
0·210	0·0219	32·7	1·50	0·156	32·6	0·350	0·0364	542
0·700	0·0729	32·8	2·00	0·208	30·8	0·700	0·0729	544
0·790	0·0822	32·9	3·86	0·402	29·2			

* 20% Aqueous EtOH in this and subsequent tables refers to an aqueous solution containing 20% by volume of ethyl alcohol.

TABLE II.

Reaction medium, 20% aqueous EtOH; k = first-order rate constant; $c = 0{\cdot}0729$ mol./l.; c_A = acid concentration in mols./l.; H_0 = Hammett's acidity function for aqueous solution.

$t = 30{\cdot}0°$.

Catalyst.	pH.	$k \times 10^4$ (min.$^{-1}$).	$10^4k/c_A$.	Catalyst.	pH.	$k \times 10^4$ (min.$^{-1}$).	$10^4k/c_A$.
0·012M-HCl + 0·04M-KCl	1·81	0·770	64	0·2M-HCl + 0·04M-KCl	1·41	14·0	70
0·032 ,, ,,	1·70	2·06	64	0·4 ,, ,,	1·35	32·9	82
0·08 ,, ,,	1·54	5·13	64				

Catalyst.	H_0.	$k \times 10^4$ (min.$^{-1}$).	$10^4k/c_A$.	$1{\cdot}09H_0 + \log 10^4k$.	Catalyst.	H_0.	$k \times 10^4$ (min.$^{-1}$).	$10^4k/c_A$.	$1{\cdot}09H_0 + \log 10^4k$.
0·02M-HCl	+1·80	1·19	60	2·04	0·02M-H_2SO_4	+1·85	1·50	75	2·19
0·1 ,,	1·05	6·25	63	1·87	0·1 ,,	1·15	7·20	72	2·11
0·2 ,,	0·69	13·4	67	1·87	0·2 ,,	0·90	15·2	76	2·16
0·4 ,,	0·38	32·8	82	1·94	0·8 ,,	0·20	85·0	110	2·15
0·6 ,,	0·23	58·0	97	2·02	1 ,,	0·10	152	150	2·09
1 ,,	−0·05	111	110	1·99	2 ,,	−0·60	635	320	2·15
2 ,,	−0·60	544	170	2·09					
3 ,,	−0·95	1350	450	2·09					
4 ,,	−1·20	3700	930	2·26					

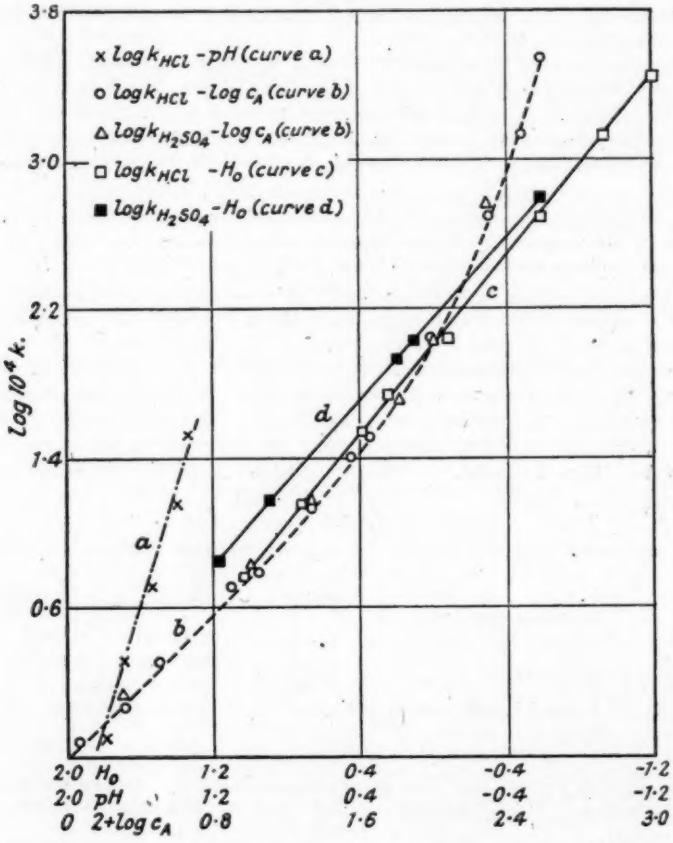
$t = 60{\cdot}0°$.

Catalyst.	$k \times 10^4$ (min.$^{-1}$).	Catalyst.	$k \times 10^4$ (min.$^{-1}$).	Catalyst.	$k \times 10^4$ (min.$^{-1}$).
0·1M-AcOH + 0·1M-AcONa + 1·5M-LiCl	0·080	0·1M-AcOH	1·3	0·1M-H_3PO_4	32·0
0·4M-AcOH + 0·4M-AcONa + 1·2M-LiCl	0·073	0·4M- ,,	3·9	0·4M- ,,	69·9
1M-AcOH + 1M-AcONa + 0·6M-LiCl	0·078	1M- ,,	4·5	1M- ,,	225

intensity of light absorption of the reaction mixture compared with that of the pure rearrangement product. In hydrochloric acid media where the acid concentration exceeds 1M, it appears that the corresponding chloride is actually the first reaction product, but is rapidly hydrolysed to the carbinol (forthcoming paper).

Analysis of the preliminary data given by Jones and McCombie (*loc. cit.*) seemed to indicate a proportionality between log k (where k is the first-order velocity constant of the reaction) and the pH value of the solution. It was desirable, as a first step, to establish whether this was indeed the case or whether k was proportional to c_A (where c_A is the stoicheiometric concentration of acid), which is the more common type of behaviour in acid-catalysed reactions (see Bell, "Acid–Base Catalysis," Oxford Univ. Press, 1942). Table II and Fig. 1, where log k is plotted against both log c_A and the electrometrically determined pH for a series of hydrochloric acid–potassium chloride mixtures in which the pH varies much more slowly than log c_A, show that k is strictly

FIG. 1.



proportional to c_A up to $c_A = 0{\cdot}1$M (*i.e.*, the plot of log k against log c_A has unit slope) and not to the thermodynamic hydrogen-ion activity measured by the pH. The primary salt effect is thus smaller than the experimental erorr (*i.e.*, $< 1\%$) for 0·04M-potassium chloride, and only amounts to 10% for 0·4M-potassium chloride (see below). The "spontaneous" rate is zero, no measurable rearrangement occurs in the absence of acid and the k–c_A plot (Fig. 1) passes through the origin.

At higher acid concentrations (both of hydrochloric and sulphuric acid) the rate becomes proportional to Hammett's acidity function (H_0), which is a measure of the tendency of the medium to donate a proton to a neutral base (Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 827; Hammett, "Physical Organic Chemistry," McGraw Hill, 1941). The H_0 values actually apply to purely aqueous solution whereas the rate constants were determined in aqueous alcohol. The plot is nevertheless justified because experiments in media of varying alcohol content show (forthcoming paper) that the relative values of the k's for different concentrations of acid are only inappreciably affected by extrapolating to zero alcohol content of the medium.

The above results appear to indicate specific hydrogen-ion * catalysis. However, the interpretation of the variation of rate with catalyst concentration and catalyst activity respectively is still a matter of controversy and it seemed imperative to apply a more generally accepted criterion to confirm the absence of general acid catalysis at low acidities. Such a criterion is provided by the dependence of the reaction rate on the total concentration of a true buffer. The range of available standard buffer mixtures conforming to the condition

* We shall employ the term "hydrogen-ion" to denote the mixture of lyonium ions present in the solution.

already enumerated for the choice of solvent is very restricted; *e.g.*, appreciable ethyl acetate formation takes place in sodium acetate–hydrochloric acid buffers containing 20% by volume of alcohol. Recourse was finally had to sodium acetate–acetic acid buffers in which the speed of reaction is very low and only the first 10% of the course of the reaction could conveniently be followed, but ester formation as measured by the alkalimetrically-determined decrease in acidity of the solution was practically absent. The velocity constants obtained under these conditions may not be trustworthy to more than ± 5%, but they suffice to show (Table II) that the rate is independent of the acetate concentration in a series of solutions of almost constant hydrogen-ion concentration (the hydrogen-ion concentration of a true buffer at constant ionic strength being almost independent of the dilution), thus confirming specific hydrogen-ion catalysis. This conclusion is further illustrated by the fact that in contrast to the results obtained with " strong " electrolytes (hydrochloric and sulphuric acid), in the case of " weak " electrolytes (phosphoric and acetic acid), k increases more slowly than c above c_A = 0·1M because the weak acids exert their own buffer action at high concentrations (see below). In anhydrous acetic acid, which contains practically no hydrogen ion, the rate of rearrangement is immeasurably slow.

In a series of eight weak acids of different charge types, the rate constants can be expressed by

$$\log k = 0{\cdot}58 \log K_A + 2{\cdot}05 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k is the first-order constant (min.$^{-1}$) in a 20% alcoholic solution of acid (1M) at 30° and K_A is the thermodynamic dissociation constant of the acid in water (taken from Landolt–Börnstein, " Tabellen ") (Table III, Fig. 2). The investigation could not be extended to certain other aliphatic, and to aromatic acids,

TABLE III.

Reaction medium, 20% aqueous EtOH; c = 0·0729 mol./l.; catalyst concentration = 1M; t = 30·0°; k = first-order rate constant; K_A = acid dissociation constant; log $k_{calc.}$ = 2·05 + 0·58 log K_A.

Catalyst.	K_A.	$k_{obs.} \times 10^4$ (min.$^{-1}$).	$k_{calc.} \times 10^4$ (min.$^{-1}$).	Catalyst.	K_A.	$k_{obs.} \times 10^4$ (min.$^{-1}$).	$k_{calc.} \times 10^4$ (min.$^{-1}$).
$KHSO_4$	$1{\cdot}2 \times 10^{-2}$	20 *	8·6	Tartaric acid	$1{\cdot}0 \times 10^{-3}$ †	2·08	2·0
$(CO_2H)_2$	$6{\cdot}5 \times 10^{-2}$ †	13·4	23	Citric acid	$8{\cdot}3 \times 10^{-4}$ †	1·41	1·8
H_3PO_4	$7{\cdot}5 \times 10^{-3}$ †	8·60	6·5	$H{\cdot}CO_2H$	$1{\cdot}8 \times 10^{-4}$	0·665	0·76
$CH_2Cl{\cdot}CO_2H$	$1{\cdot}4 \times 10^{-3}$	1·48	2·4	AcOH	$1{\cdot}8 \times 10^{-5}$	0·170	0·20

* Extrapolated value. † First ionisation.

FIG. 2.

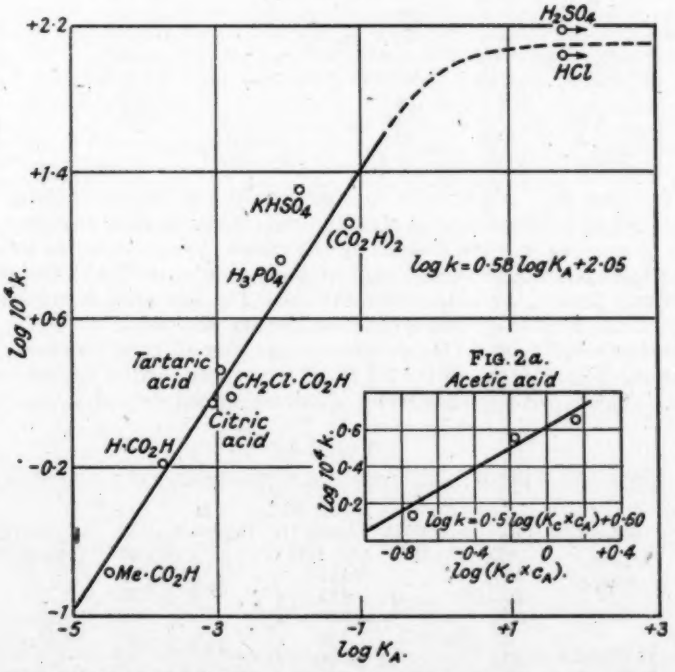


FIG. 2a.

because of the ease of esterification of the former and the high-intensity light absorption of the latter. Second and third dissociation constants of the polybasic acids could be neglected since the error thus introduced is much smaller than the average deviation. Equation (1) is identical in form with the Brönsted relation for general acid catalysis, but no statistical corrections have been applied in the present case. Theoretically, since

$$K_A = [H^+][A^-]/[HA] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(activity coefficients being neglected) and $[H^+] = [A^-]$ in the absence of salts, then

$$\log [H^+] = 0{\cdot}5 \log K_A + 0{\cdot}5 \log [HA] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

At constant acid concentration [HA] can be regarded as constant in a series of weak acids where $K_A < 10^{-3}$, and in a reaction specifically catalysed by H^+, $k = [H^+] \times$ constant, hence

$$\log k = 0{\cdot}5 \log K_A + \text{constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The slight discrepancy between the theoretical exponent of 0·5 and the observed one of 0·58, and the deviations from linearity in the plot are not surprising, since dissociation constants in water were used whereas the reaction medium actually contained 20% of alcohol, and the relative strengths of aliphatic acids vary in different solvents (Hammett, *Trans. Faraday Soc.*, 1938, **34**, 156). For stronger acids when $K_A > 10^{-3}$, the slope of the log k–log K_A curve will decrease (since [HA] is decreasing), until for strong acids when [HA] $\rightarrow 0$ and $K_A \rightarrow \infty$ it becomes almost parallel to the x axis.

The high acid concentration (1M) was chosen for comparing the catalytic activity of different acids because, at lower concentrations within the range of applicability of the Debye–Hückel theory, the reaction rates are too slow for convenient measurement at moderate temperatures. The relation (4) thus holds even at high ionic strengths at which both k/c_A (the so-called catalytic constant) and the concentration dissociation constant (K_c) of the acid are no longer constants and vary to a different extent with the concentration (c_A) for different acids. The condition for this follows from (2), which becomes

$$\log k = 0{\cdot}5 \log (K_A c_A) + \text{constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

when $c_A \approx$ [HA]. Equation (5) is satisfied in the case of acetic acid (Fig. 2*a*) where the relevant K_c values are available (Falkenhagen, " Elektrolyte," 1932, p. 32).

The accuracy of the kinetic measurements does not at present warrant an investigation of salt effects at low salt concentrations. At high ionic strengths the primary salt effect is positive (Table IV), and again proportional

TABLE IV

Reaction medium, 20% aqueous EtOH; $t = 30{\cdot}0°$; $c = 0{\cdot}0729$ mol./l.; k_A = first-order rate constant in presence of acid only; k_S = first-order rate constant in presence of salt; r = % increase in k due to added salt = $100(k_S - k_A)/k_A$.

Catalyst.	$k_A \times 10^4$ (min.$^{-1}$).	$k_S \times 10^4$ (min.$^{-1}$).	r.	Catalyst.	$k_A \times 10^4$ (min.$^{-1}$).	$k_S \times 10^4$ (min.$^{-1}$).	r.
0·4M-HCl + 0·4M-KCl	32·9	36·3	10·3	0·4M-HCl + 0·5M-$BaCl_2$	32·9	56·0	70·0
,, 0·6 ,,	,,	40·2	22·5	,, 1M-KBr	,,	55·5	68·8
,, 0·8 ,,	,,	49·9	51·7	,, 1M-LiCl	,,	55·3	68·0
,, 1·0 ,,	,,	52·9	60·8	,, 1M-NaCl	,,	55·3	68·0
,, 1·2 ,,	,,	60·8	84·8	,, 0·5M-$ZnCl_2$	,,	53·0	61·1
,, 1·6 ,,	,,	62·5	90·0	,, 1M-KCl	,,	52·9	60·8
,, 1·8 ,,	,,	65·3	98·3	,, 1M-NH_4Cl	,,	49·0	48·9
,, 2·0 ,,	,,	76·8	134	,, 0·33M-$AlCl_3$	,,	45·4	38·0
0·1M-HCl + 1M-KCl	6·25	11·0	76·0	,, 1M-$AlCl_3$	,,	134	307
0·4M ,, ,,	32·9	52·9	60·8	1M-H_3PO_4 + 1M-KCl	8·6	17·8	107
1·0M ,, ,,	111	164	47·8	1M-AcOH ,,	0·170	0·370	118

to Hammett's acidity function H_0. It decreases with increasing acid concentration in the case of hydrochloric acid. The effects produced by different salts at constant ionic strength show a rough parallelism to the activity coefficients of the salts in aqueous solution divided by the molar concentrations in which they are present, but bear no relation to their co-ordinating powers, thus illustrating once more that hydrogen ion is the only effective catalyst (cf. Bodendorf and Böhme, *Annalen*, 1935, **516**, 1). The salt effect is much higher in the case of the weak acids owing to the simultaneous operation of the secondary salt effect.

Rate constants were measured over the temperature range from 0° to 60°, and obey an Arrhenius equation (Table V). The deviations from linearity of the log k–$1/T$ plots only slightly exceed those to be expected from the probable error in k. The experimental energies of activation deduced vary from 19 to 24 ($\pm$ 0·3) kg.-cals.

TABLE V

Reaction medium: 20% aqueous EtOH; $c = 0{\cdot}0729$ mol./l. throughout; E = Arrhenius energy of activation.

t.	Catalyst.	$k \times 10^4$ (min.$^{-1}$).	E (kg.-cals.).	t.	Catalyst.	$k \times 10^4$ (min.$^{-1}$).	E (kg.-cals.).	t.	Catalyst.	$k \times 10^4$ (min.$^{-1}$).	E (kg.-cals.).
30°	0·1M-HCl	6·25	23·2	0°	1M-HCl	1·73	24·2	30°	0·2M-H_2SO_4	15·2	23·8
40	,,	21·0		30	,,	111		40	,,	52·9	
50	,,	64·4		40	,,	415		50	,,	159	
60	,,	220		50	,,	1230		60	,,	550	
30	0·4M-HCl	32·9	23·5	0	4M-HCl	106	19·4	30	1M-H_3PO_4	8·60	21·6
40	,,	122		30	,,	3700		60	,,	225	
50	,,	330						30	1M-AcOH	0·170	22·2
								40	,,	0·521	
								50	,,	1·60	
								60	,,	4·49	

over a very wide range of acidities, but in calculating experimental energies of activation from the overall temperature coefficients of the reaction, no allowance is made for the temperature-dependence of acid strength.

In 0·4M-hydrochloric acid the rate of racemisation of (+)propenylethynylcarbinol ($[\alpha]_D^{20°} = +45°$) as determined by the change in optical rotation is almost the same as the rate of rearrangement as measured by

the change in ultra-violet light absorption, the two values of k being $27{\cdot}5 \pm 1{\cdot}5$ and $30{\cdot}8 \pm 0{\cdot}6 \times 10^{4}$ min.$^{-1}$ respectively. Under the experimental conditions employed, complete racemisation was observed.

Experimental.

Kinetic Measurements.—The reactions were carried out in 50 ml. of reaction medium contained in 150-ml. Pyrex three-necked flasks. The centre neck carried a glass-joint double-surface condenser, one side neck was fitted with an inlet tube for passing a slow stream of nitrogen through the solution, and the second side neck carried a glass stopper and was used for the withdrawal of samples. The precaution of carrying out the reaction in nitrogen was later found to be unnecessary, propenylethynylcarbinol and its isomer being quite stable in aqueous-alcoholic solution for periods exceeding the duration of the experiments (the stability depends on the acidity of the solution and the temperature, ranging from 1 to 2 days in 4M-hydrochloric acid at 30° to periods exceeding 2 weeks in 0·01M-hydrochloric acid before any detectable decomposition occurs).

Four reaction flasks were kept in a rectangular water tank of 20 l. capacity, kept at constant temperature by means of a large bulb toluene–mercury thermoregulator, electronic valve relay, and a 250-watt carbon-filament lamp, and an electric stirrer. For experiments above 50°, an 800-watt resistance heating element was substituted for the lamp, and a thin layer of paraffin oil was spread over the water surface to reduce evaporation. Temperatures were checked against an N.P.L. certificated thermometer and were constant within $< \pm 0{\cdot}05°$. Runs at 0° were carried out in a tightly stoppered 150-ml. flask immersed in a large volume of a mixture of ice and water, the whole being kept in a refrigerator at 0°.

To start a run, a sample of propenylethynylcarbinol previously weighed out into a short sample tube was dropped into the reaction flask already containing the reaction medium at the temperature of the run, the stopper replaced, and the flask vigorously shaken until the contents were homogeneous, the whole operation requiring less than 5 secs. Samples of the reaction mixture were then withdrawn at appropriate intervals by means of a fast-delivery, narrow-stem 1-ml. pipette and run into a graduated flask (25—100 ml.) containing sufficient dilute alcoholic potassium hydroxide to neutralise the 1 ml. of reaction medium, and the volume made up to the mark. The use of a small-capacity pipette has the twofold advantage of (i) allowing the withdrawal and discharge of the sample to be completed within 10 seconds (with an error of within $\pm 0{\cdot}5\%$)—this was essential as the half-time of reaction of the fastest runs was only 4 minutes—and (ii) permitting a high and variable dilution ratio which makes it possible to combine in one operation the stopping of the reaction and the dilution to a suitably low concentration for spectrographic examination.

The spectrophotometric assay was carried out by standard methods on a Hilger medium quartz spectrograph (E488) fitted with a Spekker photometer using a condensed spark between tungsten-steel electrodes as light source. Freshly distilled propenylethynylcarbinol has an intensity of light absorption at 2235 A. of $E^{1\%}_{1\,cm.} < 2$, whereas its rearranged isomer hex-3-en-5-yn-2-ol has a maximum at 2235 A. of $E^{1\%}_{1\,cm.} = 1300$. For readings above $E^{1\%}_{1\,cm.} = 100$ the amount of rearrangement is therefore directly proportional to the $E^{1\%}_{1\,cm.}$ value of the solution (using the reaction medium at the same dilution in the comparison cell). The accuracy of the determination of extinction coefficients by this method is not better than ± 2—5% for general work in this wave-length region, but by employing standard conditions, accurate blank determinations, and interpolation to $0{\cdot}01E$, it is possible to obtain results within $\pm 1\%$. Together with errors arising from pipetting, etc., the total traceable error should not exceed $\pm 2\%$. This corresponds to a maximum error of $\pm 0{\cdot}5$—3% in the first-order velocity constants calculated by $k = (2{\cdot}3/\tau)\log_{10}a/(a - x)$ for $x = (0{\cdot}15$—$0{\cdot}85)a$ within one run. Runs in which variations in k exceeded $\pm 5\%$ were rejected. Consistency between averaged k values for different runs is greatly dependent on the accuracy of the value for a (the $E^{1\%}_{1\,cm.}$ value of the fully rearranged carbinol); this was averaged from a large number of determinations as $E^{1\%}_{1\,cm.}$ (2235 A.) $= 1300 + 0{\cdot}5(t - 30)$ for the pipette employed, where t is the temperature of the run. The slight variation in this value with t is mainly due to thermal expansion of the pipette, but since the absolute values are immaterial in the calculation of first-order constants, the pipette was not recalibrated in absolute units for sampling at different temperatures. Averaged k values should thus be within ± 2—3%; agreement between duplicate runs was generally better than this. A few typical runs are given below:

Reaction medium: 20% (vol.) EtOH, 80% (vol.) H_2O throughout; $E^{1\%}_{1\,cm.}$ at 2235 A.; time in mins., and k in min.$^{-1}$ throughout.

(i) Catalyst: 0·4M-HCl; c = 0·0822 mol./l.; t = 30·0°.

	Time.	$E^{1\%}_{1\,cm.}$	$k \times 10^4$.
(a)	60	232	32·7
	120	431	33·7
	240	715	33·2
	360	885	31·6
	480	1010	31·3
	∞	1300	
		Mean	32·5
(b)	60	234	33·0
	120	436	33·9
	240	728	34·1
	360	905	32·9
	480	1030	32·8
	∞	1300	
		Mean	33·3

(ii) Catalyst: 1M-HCl; c = 0·0729 mol./l.; t = 30·0°.

Time.	$E^{1\%}_{1\,cm.}$	$k \times 10^4$.
40	468	111
72	715	111
137	1015	110
∞	1300	
	Mean	111

(iii) Catalyst: 4M-HCl; c = 0·0729 mol./l.; t = 30·0°.

Time.	$E^{1\%}_{1\,cm.}$	$k \times 10^4$.
2	700	3860
4	985	3550
6	1160	3700
∞	1300	
	Mean	3700

(iv) Catalyst: 1M-HCl; c = 0·0729 mol./l.; t = 40·0°.

Time.	$E^{1\%}_{1\,cm.}$	$k \times 10^4$.
16·5	642	415
22·5	788	413
29·0	914	417
∞	1305	
	Mean	415

(v) Catalyst: 1M-AcOH; c = 0·0729 mol./l.; t = 50·0°.

Time.	$E^{1\%}_{1\,cm.}$	$k \times 10^4$.
1500	280	1·62
2940	500	1·65
4320	660	1·64
6960	845	1·51
∞	1310	
	Mean	1·60

Three to five individual values of k were determined in each run, as far as possible in the region $x = (0{\cdot}30$—$0{\cdot}70)a$ where the relation between the error in $E^{1\%}_{1\,cm.}$ and k is most favourable. End values (a), when determined, were taken after not less than ten times the time of half-change, corresponding to more than 99·9% rearrangement. In slow runs, a was determined, where possible, by warming for the appropriate period to complete the reaction. In all cases the value of a taken for the calculation of k was the averaged value, $1300 + 0{\cdot}5(t - 30)$. The smallest velocity constant measured was $0{\cdot}08 \times 10^{-4}$ min.$^{-1}$, the largest 3700×10^{-4} min.$^{-1}$, corresponding to times of half-change of 50 days and 2 minutes respectively.

A few runs were carried out with resolved (+)propenylethynylcarbinol, and the rearrangement followed by observing the change in optical rotatory power as well as in light absorption. 1-Ml. samples of the reaction mixture were run into an equal volume of alcoholic potassium hydroxide, and the rotation determined in a semi-micro 1-dcm. cell, a sodium-

vapour lamp being used as light source. The low rotations measured did not permit of great accuracy, but the results suffice to establish the essential identity of the velocity constants determined by the two methods and the fact that complete racemisation accompanies the rearrangement under the conditions of the experiment.

Medium, 20% (vol.) EtOH, 80% (vol.) H_2O; catalyst, 0·4M-HCl; c = 0·208 mol./l.; t = 30·0°.

Time (mins.)	16	136	197	254	331	∞	
$\alpha_D^{20°}$	0·53°	0·39°	0·34°	0·25°	0·215°	0·00°	
$k \times 10^4$ (min.$^{-1}$)	—	25·5	24·5	31·0	28·5	—	Mean 27·5

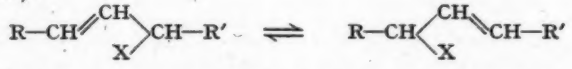
Analysis of Reaction Products.—In view of the wide range of conditions employed, it was necessary to confirm that the reaction product in every case was in fact the rearranged carbinol, as established by Jones and McCombie (*loc. cit.*) for the heterogeneous rearrangement, and not the corresponding ester, ether, etc. Some guidance is provided by the $E_{1\,cm.}^{1\%}$ end value *a* which is somewhat different for the carbinol and its various derivatives, but in a number of representative runs the final reaction product was isolated and examined by means of refractive index, Zerewitinoff, Zeisel, and chloride determinations. Evidence of ester formation was sought for, especially in the case of acetic acid runs, by titration of the reaction mixture with standard sodium hydroxide. No products other than the rearranged carbinol were detected in appreciable quantities under any of the conditions investigated except in hydrochloric acid media of acid concentration exceeding 1M where 2-chlorohex-3-en-5-yne is formed in increasing amounts as primary reaction product, but this is hydrolysed to the carbinol at a rate comparable to that of the rearrangement. Small amounts of ethyl acetate and ethyl chloroacetate (corresponding to < 10% of the acid present) were formed in acetic acid and chloroacetic acid runs, and small amounts of diethyl ether were produced when phosphoric acid was used as catalyst.

pH *Determinations.*—These were carried out by measuring the E.M.F.'s of cells H_2(Pt)|HCl–KCl soln.|satd.KCl bridge|1·0N-KCl–$HgCl_2$, the pH of the solution being given by pH = (E.M.F. − 0·283)/0·0058, liquid junction potentials being neglected. The hydrogen electrode was of the enclosed vessel type. E.M.F.'s were determined with a Hinsley potentiometer and moving-coil galvanometer to ± 1 mv. corresponding to about ± 0·02 pH unit. Steady conditions were attained after 30—60 minutes. Checking against a standard acetate buffer and hydrochloric acid–potassium chloride mixture gave agreement within 0·02 pH. The values obtained for the 20% alcoholic hydrochloric acid–potassium chloride mixtures differ considerably from Clark and Lubs's values for purely aqueous solutions.

Materials.—The propenylethynylcarbinol (for which we thank Mr. B. C. L. Weedon) had b. p. 82°/46 mm., $n_D^{20°}$ = 1·4647, $E_{1\,cm.}^{1\%}$ at 2235 A. < 2, this value being unchanged after 3 months at 0°. We are indebted to Dr. J. Kenyon, F.R.S., for a sample of resolved propenylethynylcarbinol ($[\alpha]_D^{20°}$ + 45°). Burnett's absolute alcohol was used throughout the investigation. All other materials were "AnalaR" reagents or were purified by standard methods. A. R. Borax, dried and kept in a desiccator over anhydrous silica gel, was used as primary volumetric standard.

Discussion.

Previous discussion of anionotropic rearrangements * has centred about two types of mechanism: an intermolecular, ionic mechanism (Burton and Ingold, *loc. cit.*), $CHR{:}CH{\cdot}CHXR^1 \rightleftharpoons CHR{:}CH{\cdot}\overset{+}{C}HR^1 + X^- \rightleftharpoons \overset{+}{C}HR{\cdot}CH{:}CHR^1 + X^- \rightleftharpoons CHRX{\cdot}CH{:}CHR^1$, and an intramolecular homopolar mechanism (Kenyon, Partridge, and Phillips, *loc. cit.*)



These mechanisms were originally proposed in connection with anionotropic rearrangements in the arylallyl alcohol series, evidence for the former being derived mainly from qualitative data on the dependence of the ease of rearrangement on the electronic properties of R, R^1, and X, the ionising power of the solvent, and the exchange of X for other anions during rearrangement. Evidence for the intramolecular mechanism was obtained mainly from investigations of the stereochemical changes accompanying rearrangement. It has been suggested that the partial racemisation observed during the rearrangement of α-phenyl-γ-methylallyl alcohol in solvents of low ionising power is due to the simultaneous operation of both mechanisms (Hughes, *Trans. Faraday Soc.*, 1941, **37**, 601).

The salient experimental facts relating to the oxotropic rearrangement of propenylethynylcarbinol and our interpretations of them are as follows:

(i) In 20% aqueous alcohol the rearrangement is of the first order, the rate constant being independent of the concentration of carbinol and directly proportional to the hydrogen-ion concentration at low acidities. At high concentrations of strong acids and in the presence of salts, the rate becomes proportional to Hammett's acidity function, which is a measure of the tendency of the medium to donate a proton to a neutral base. The rate constants in solutions of different acids at constant concentration can be expressed by $k = K_A{}^x +$ a constant, where the exponent x has a value close to the theoretical one of 0·5 for specific hydrogen-ion catalysis.

Hydrogen-ion is the effective catalyst. The transition state of the reaction does not involve a solvent molecule (cf. Hammett, *loc. cit.*).

(ii) No products other than the rearranged carbinol are formed at acid concentrations as high as 1M-hydrochloric or acetic acid.

If the hydroxyl group separates as a charged anion, the rearrangement must be intramolecular with respect to other anions present.

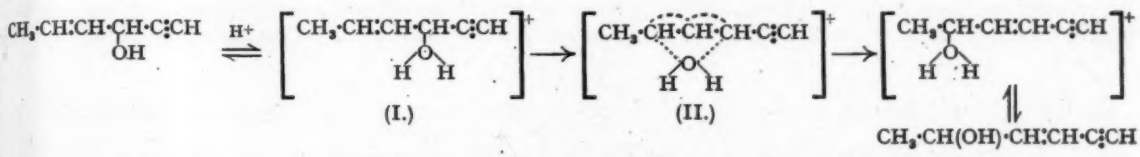
(iii) Under the particular conditions examined, the isomerisation of the optically active carbinol is accompanied by complete racemisation proceeding at the same rate.

* We propose the name "oxotropy" for anionotropic changes where X = OH, corresponding to the term "prototropy" for cationotropic changes where X = H.

Two possibilities have to be considered. Either the carbonium ion produced by the fission of the carbon–oxygen bond is optically stable and the racemisation is brought about by the actual electronic rearrangement, or the reaction involves the production of an optically unstable carbonium ion and the fission of the carbon–oxygen bond proceeds simultaneously with the electron migration. The optical instability of *positive* carbonium ions now appears to be generally accepted (Waters, "Physical Aspects of Organic Chemistry," Routledge, 1942, p. 340), and the second interpretation must be regarded as correct.

(iv) The experimental energy of activation varies from 19 to 24 kg.-cals. over a wide range of acidities. Unless the true energy of activation is very much higher than the experimental value, the rate-determining step of the reaction can involve neither the normal covalent nor the normal ionic fission of the carbon–oxygen bond.

Clearly the above conclusions are not wholly in accord with either of the two types of mechanism referred to above. They can be explained, however, in terms of the following mechanism which includes elements of both:



The first step is the reversible formation of the oxonium ion (I), the existence of which in acid solution would be postulated quite independently of the reaction it subsequently undergoes, as has been emphasised already by Young and Lane (*loc. cit.*) in their discussion of anionotropic rearrangements accompanying replacement halogenations. The second step is the *simultaneous* migration of the double-bond electron pair and the hydroxyl group as a neutral water molecule. The transition state in which both migrations are half completed is represented by (II). The essential rôle of the hydrogen-ion catalyst is thus to lower the energy of activation by converting the rate-determining step from a fission of the carbon–oxygen bond into two ions, into the fission of the carbon–oxygen bond into a carbonium ion and a neutral molecule. Such a mechanism brings this case of acid catalysis into line with the general principle that the main function of a catalyst is to provide an alternative reaction path with a lower energy of activation. On this basis the reaction is clearly intramolecular with respect to other anions present in the solution; it is probably intramolecular with respect to the solvent also, but the latter point requires confirmation, *e.g.*, by carrying out the reaction in a medium enriched with ^{18}O.

The further discussion of the mechanism proposed above and its implications is deferred until data are available as to the effect of solvents and substituents on the reaction rate and the energy of activation.

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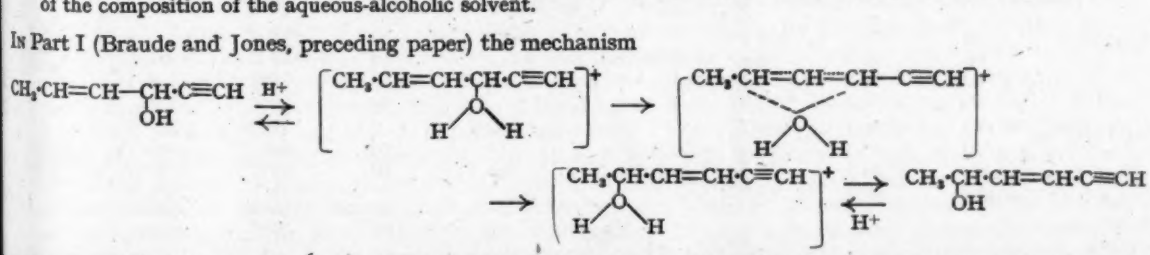
119. *The Kinetics of Anionotropic Rearrangement. Part II. Medium Effects in the Oxotropy of Propenylethynylcarbinol. The Determination of Isodielectric Energies of Activation.*

By ERNEST A. BRAUDE.

Further evidence is adduced for the reaction mechanism proposed in Part I from a study of the effect of varying the alcohol content of the reaction medium on the rate of reaction and energy of activation. The rearrangement of the oxonium ion ROH_2^+, not the preceding proton-transfer reaction, appears to be the rate-determining step. A method is outlined for the calculation of isodielectric energies of activation, the values obtained being 4 to 10 kg.-cals. higher than the experimental energies of activation and practically independent of the composition of the aqueous-alcoholic solvent.

In Part I (Braude and Jones, preceding paper) the mechanism



was proposed for the rearrangement of propenylethynylcarbinol, as the result of an investigation of the kinetics of the reaction in aqueous solution containing 20% by volume of ethyl alcohol. It appeared worth while to extend the investigation to other ethyl alcohol–water mixtures, both for the intrinsic interest of the dependence of reaction rate on medium composition and the additional evidence it would provide concerning the reaction

mechanism. The effect of change of solvent on a catalysed reaction is, of course, composite in nature, affecting the reaction (*a*) directly and (*b*) indirectly through the catalyst, *e.g.*, by altering its acid or base strength. These two types of effect are somewhat analogous to the salt effects encountered in catalysed reactions, and will be referred to as *primary and secondary solvent effects*. This aspect of catalysed reactions has so far received but little attention. The study of solvent effects in two-component media seems particularly important in the case of catalysed reactions, because, as will be shown below, it allows the determination of isodielectric energies of activation, *i.e.*, energies of activation calculated for a reaction medium of temperature-invariant dielectric constant. These are a better estimate of the true energy of activation than the values obtained by the direct application of the Arrhenius equation, and are likely to differ from the latter to a particularly large extent in reactions catalysed by substances themselves subject to a thermodynamic equilibrium.

(A) *The Variation of Rate Constants with Medium Composition.*—The relevant data are collected in Table I. In the range 20—80% by volume alcohol content the rate constants at constant acid concentration decrease rapidly with increasing alcohol concentration and decreasing dielectric constant of the solvent (hex-3-en-5-yn-2-ol remaining the sole reaction product), an increase by 20% of the alcohol content decreasing the rate by a nearly constant factor of *ca.* 3 when strong, and of *ca.* 4 when weak acids are employed as catalysts. The

TABLE I.

k = first-order rate constant (in min.$^{-1}$); D = dielectric constant of solvent; $\log k = mD + n$. Concentration of carbinol = 0·0729 mol./l. throughout.

Catalyst.	Solvent (vol.-% EtOH).	D.	10^4k.		Catalyst.	Solvent (vol.-% EtOH).	D.	10^4k.	
			$t = 30{\cdot}0°$.						
0·1M-HCl	20	67·7	6·25		0·4M-HCl	20	67·7	32·8	
	40	57·6	2·09	$m = 0{\cdot}0469$		40	57·6	10·5	$m = 0{\cdot}0439$
	60	46·3	0·583	$n = -2{\cdot}39$		60	46·3	3·25	$n = -1{\cdot}49$
	80	34·6	0·210			80	34·6	1·12	
1M-HCl	20	67·7	111		4M-HCl	20	67·7	3700	
	40	57·6	43·1	$m = 0{\cdot}0385$		30	62·7	2600	
	60	46·3	15·3	$n = -0{\cdot}581$		40	57·6	1440	
	80	34·6	5·07			60	46·3	1060	
	90	29·0	4·90						
	100	23·5	47·1						
			$t = 40{\cdot}0°$.						
0·1M-HCl	20	64·4	21·0		1M-HCl	20	64·4	415	
	40	54·6	7·70	$m = 0{\cdot}0468$		40	54·4	164	$m = 0{\cdot}0419$
	60	43·9	2·22	$n = -1{\cdot}569$		60	43·9	49·7	$n = -0{\cdot}095$
	80	32·6	0·851			80	32·6	21·8	
0·4M-HCl	20	64·4	122			90	27·2	21·8	
	40	54·6	33·8	$m = 0{\cdot}0444$		100	22·0	156	
	60	43·9	13·6	$n = -0{\cdot}795$					
	80	32·6	4·57						
			$t = 50{\cdot}0°$.						
0·1M-HCl	20	61·5	64·4		0·4M-HCl	20	61·5	330	
	40	52·1	22·0	$m = 0{\cdot}0420$		40	52·1	149	$m = 0{\cdot}0393$
	60	41·4	8·10	$n = -0{\cdot}823$		60	41·4	42·9	$n = -0{\cdot}075$
	80	31·0	3·19			80	31·0	20·0	
	85	28·3	2·42		1M-HCl	20	61·5	1230	
	90	25·8	2·29			40	52·1	517	$m = 0{\cdot}0400$
	95	23·1	2·98			60	41·4	172	$n = 0{\cdot}612$
	100	20·5	15·6			80	31·0	72·9	
						85	28·3	75·1	
						90	25·8	77·0	
						100	20·0	471	
			$t = 60{\cdot}0°$.						
0·1M-HCl	20	59·2	220		1M-H_3PO_4	20	59·2	225	
	40	49·7	56·8	$m = 0{\cdot}0393$		40	49·7	66·8	$m = 0{\cdot}0528$
	60	38·3	28·1	$n = -0{\cdot}119$		60	38·3	15·8	$n = -0{\cdot}802$
	80	29·3	10·0			80	29·3	2·72	
0·2M-H_2SO_4	20	59·2	550		1M-AcOH	0	68·7	14·3	
	40	49·7	201	$m = 0{\cdot}0374$		20	59·2	4·49	$m = 0{\cdot}0621$
	60	38·3	74·5	$n = 0{\cdot}432$		40	49·7	0·995	$n = -2{\cdot}98$
	80	29·3	32·3			60	38·3	0·25	
						80	29·3	0·020	
						100	19·0	0·014	

rate constants for any one catalyst in different media at constant temperature can be accurately represented by the relation

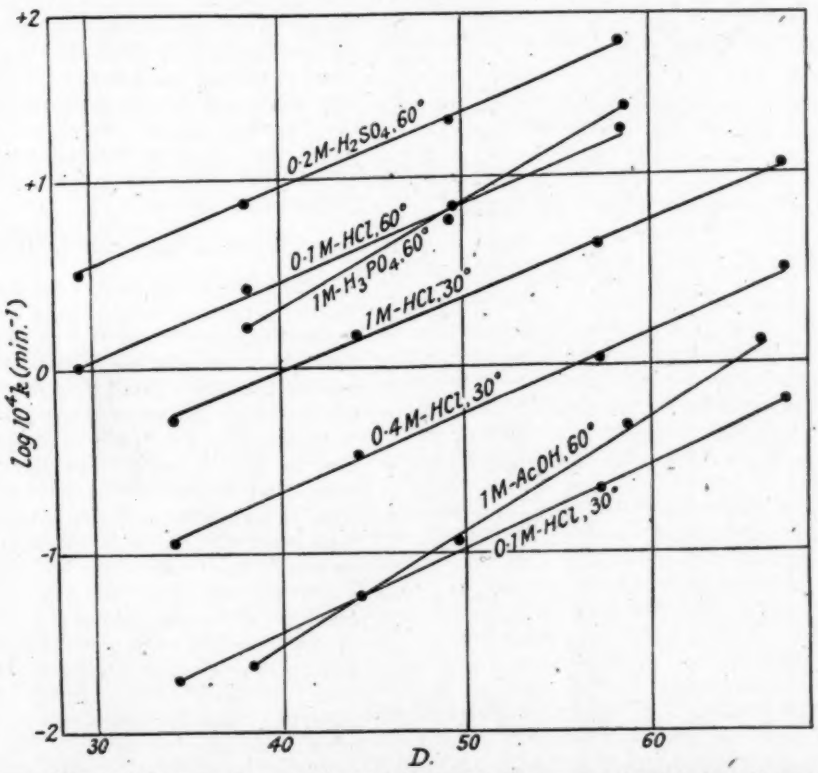
$$\log k = mD + n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where D is the dielectric constant of the alcohol–water mixture, and m and n are constants (Fig. 1); m varies

only slightly with acid concentration and temperature. In phosphoric and acetic acid, relation (1) only holds up to 60% alcohol content. In the latter case, the range of media could be extended to 0% alcohol content, propenylethynylcarbinol being sufficiently soluble in aqueous 1M-acetic acid. It may be noted that the log k–D plot is considerably more nearly linear than the log k–[EtOH] one (the [EtOH]–D plot being itself not quite linear), but that the variation in k can also be fairly satisfactorily represented by certain monotonic functions of D other than (1), such as $\log k = -p/D + q$, a form preferred by some authors on theoretical grounds. Actually, their results, as our own, are often more accurately represented by (1), and we prefer it for this reason and also because it is the most convenient relation for the calculation of isodielectric constants (see below), but no theoretical conclusions are based on this choice.

When 4M-hydrochloric acid is used as catalyst, intermediate formation of 2-chlorohex-3-en-5-yne and subsequent hydrolysis to the carbinol probably occurs, and relation (1) no longer holds.

FIG. 1.



The linear dependence of k upon D according to (1) has been encountered before in first-order reactions such as the isomerisation of camphene hydrochloride and various keto-enol transformations (Meerwein and Emster, *Ber.*, 1920, **53**, 1815; 1922, **55**, 2500; Stobbe, *Annalen*, 1903, **326**, 347; Moelwyn-Hughes, "Kinetics of Reactions in Solution," Oxford, 1933, p. 118). These investigations refer to a series of solvents rather than to change of composition in a two-component medium, but the same behaviour has been found more recently for series of water–alcohol mixtures (Hughes, J., 1935, 255; Price and Westheimer, *J. Chem. Physics*, 1943, **11**, 150) and has been interpreted by Hückel ("Theoretische Grundlagen der Organischen Chemie," Leipzig, 1931, p. 266) in terms of the dependence of the free energy of ionisation of the molecule undergoing a change on the dielectric constant of the medium. Such an interpretation is obviously valid only when the reaction mechanism actually involves a separation of two ions, whereas the present reaction, according to the mechanism proposed in Part I, involves the intramolecular fission of a carbon–oxygen bond into a carbonium ion and a neutral water molecule, the ease of which should be almost independent of the dielectric constant of the solvent.

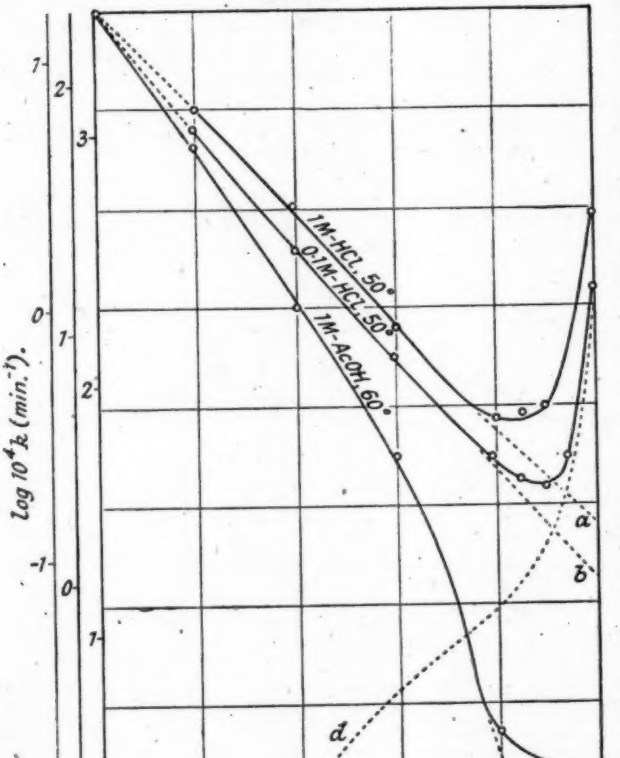
Moreover, on increasing the alcohol content of the medium beyond 80%, the rate constants in hydrochloric acid are found to pass through a minimum at *ca.* 90% alcohol content and then to increase again, while in acetic acid the log k–D curve becomes almost parallel to the x axis (Fig. 2). The exact location of the minimum in the former case depends on the acid concentration and moves towards lower alcohol content with increasing acid concentration. The rise in the rate constants in hydrochloric acid between 90% and 100% alcohol content is very steep, the rate constant in 100% alcohol being similar to that in 40% alcohol, and it is probable that still higher values could be obtained in completely anhydrous alcohol (100% alcohol refers to Burnett's "absolute alcohol" which probably contains 0·1—0·3% of water). Some 2-ethoxyhex-3-en-5-yne is formed during the rearrangement in media of high alcohol content.

This behaviour is very similar to that exhibited by acid-catalysed esterification, and the acid-catalysed decomposition of diazoacetic ester (Goldschmidt, *Z. physikal. Chem.*, 1907, **60**, 728; *Z. Elektrochem.*, 1914, **20**, 473; Fraenkel, *Z. physikal. Chem.*, 1907, **60**, 202; Kailan, *Monatsh.*, 1907, **28**, 115; Bredig, *Ber.*, 1906, **39**, 1576; Millar, *Z. physikal. Chem.*, 1913, **85**, 129; and later papers) where minima in the rate constants occur for 85—95% alcohol content of the medium, depending on the catalysing acid and its concentration. The investigations of Goldschmidt and Bredig and their collaborators were concerned mainly with the inhibiting effects of small concentrations of water on the rate of reaction in alcohol, *i.e.*, with the range of reaction medium of very high alcohol content, and led to Goldschmidt's theory of ethoxonium-ion formation, adhered to by later workers, in which the strong anti-catalytic effect of adding water to the acid–alcohol medium was explained by the concomitant decrease in the concentration of ethoxonium ions, regarded as effective catalyst. Goldschmidt defined the "hydrolytic constant" (r) as the equilibrium constant of the reaction

$$EtOH + H_3O^+ \rightleftharpoons EtOH_2^+ + H_2O$$

multiplied by the alcohol concentration, and r was shown to have a value of *ca.* 0·2 for high alcohol concentrations. From this it can be calculated that the concentration of ethoxonium ions will become negligibly small ($[EtOH_2^+]/[H_3O^+] < 0{\cdot}01$) on increasing the water content beyond *ca.* 20%. Goldschmidt's theory is now well accepted, but it may be noted that it deals only with the right hand part of the log k–alcohol content curve (Fig. 2) and gives no explanation why $EtOH_2^+$ is a far more effective catalyst than H_3O^+. It will be shown below that such an explanation is provided by regarding the present case of acid catalysis as a proton-transfer reaction, the increase of rate constant with water content on the left-hand part of the curve being accounted for mainly as a secondary solvent effect, the increase in dielectric constant resulting in an increase in effective catalyst strength.

FIG. 2.



We have to consider the following set of reactions:

(*a*) $HA + H_2O \rightleftharpoons H_3O^+ + A^-$
(*b*) $HA + EtOH \rightleftharpoons EtOH_2^+ + A^-$
(*c*) $HA + ROH \rightleftharpoons R{\cdot}OH_2^+ + A^-$
(*f*) $R{\cdot}OH_2^+ \xrightarrow{k_f} R'{\cdot}OH_2^+$

Since in dilute solution the amount of carbinol (R·OH) is small compared with that of H_2O and EtOH, we can write instead:

(*d*) $R{\cdot}OH + H_3O^+ \underset{k_{-d}}{\overset{k_d}{\rightleftharpoons}} R{\cdot}OH_2^+ + H_2O$
(*e*) $R{\cdot}OH + EtOH_2^+ \underset{k_{-e}}{\overset{k_e}{\rightleftharpoons}} R{\cdot}OH_2^+ + EtOH$

The system (*d*), (*e*), (*f*) is amenable to simple analysis. Two possibilities arise; either the proton transfer (*d*), (*e*), or the rearrangement of the oxonium ion (*f*) is rate-determining. In the latter case, the rate of reaction is given by the transition-state theory as

$$v = k_f[R{\cdot}OH_2^+] f_{R{\cdot}OH_2^+}/f_{X_f} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where k's represent rate constants, f's represent activity coefficients and X_f refers to the transition state of reaction (*f*), and the rate constant of the total reaction

$$k = v/[R{\cdot}OH] = k_f[R{\cdot}OH_2^+] f_{R{\cdot}OH_2^+}/[R{\cdot}OH] f_{X_f} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

This reduces to

$$k = \alpha k_f[R{\cdot}OH_2^+]/[R{\cdot}OH] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3a)$$

where $f_{R{\cdot}OH_2^+} = \alpha f_{X_f}$, if $f_{R{\cdot}OH_2^+}$ varies in the same way as f_{X_f} with environment, or to

$$k = k_f[R{\cdot}OH_2^+]/[R{\cdot}OH] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3b)$$

if the activity coefficients of the oxonium ion and the transition state have the same value, as is likely to be the case. We obtain the simple result that the rate constant of the reaction is equal to the rate constant of the actual rearrangement multiplied by the ratio $[R{\cdot}OH_2^+]/[R{\cdot}OH]$. Now the logarithm of this ratio is proportional to Hammett's acidity function which is defined by

$$H_0 = -\log a_{H^+} f_B / f_{BH^+} = pK_a^B - \log (c_{BH^+}/c_B) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where a_{H^+} represents the activity of the hydrogen ion and K_a^B is a constant (the equilibrium constant of the reaction $B + H^+ \rightleftharpoons BH^+$) and B is *any* neutral base (Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 827), so that at constant temperature log k should be simply proportional to H_0. This has already been shown to be the case for the variation of k with acid concentration in a constant medium (Part I); the relevant values of the acidity functions for media of varying alcohol content are not at present available, but will form the subject of a separate investigation.

If, on the other hand, the oxonium-ion formation (*d*), (*e*) were rate-determining, application of Christiansen's equation (*Z. physikal. Chem.*, 1935, *B*, **28**, 303; Hammett, "Physical Organic Chemistry," McGraw–Hill, 1941, p. 107) yields

$$k = \frac{k_d k_f a_{H_3O^+}}{k_f/f_{X_d} + k_{-d} a_{H_2O}} + \frac{k_e k_f a_{EtOH_2^+}}{k_f/f_{X_e} + k_{-e} a_{EtOH}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and approximately, since $k_f \gg k_d$, k_e on the present assumption

$$k = k_d a_{H_3O^+}/f_{X_d} + k_e a_{EtOH_2^+}/f_{X_e} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5a)$$

This reduces further to

$$k = k_d a_{H_3O^+}/f_{X_d} = k_d[H_3O^+] \times \frac{f_{H_3O^+}}{f_{X_d}} = \beta k_d[H_3O^+] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5b)$$

for a constant medium of low alcohol content where $[EtOH_2^+] \ll [H_3O^+]$ and β is the ratio of the activity coefficients of the hydroxonium ion and the transition state of reaction (*f*). Since the latter is itself an oxonium ion, β should be inappreciably affected by change in acid concentration, and the rate constants should thus be proportional to $[H_3O^+]$, *i.e.*, the stoicheiometric acid concentration. It has already been shown (Part I) that in the present reaction log k is not proportional to log c_A above $c_A = 0{\cdot}1$ or to the pH at constant alcohol concentration, nor is it proportional to the pH at constant acid concentration, as shown by a comparison with the pH values of 0·5M-hydrochloric acid solutions in alcohol–water mixtures (Millet, *Trans. Faraday. Soc.*, 1927, **23**, 515). In any case, $a_{H_3O^+}/f_{X_d}$ is not proportional to H_0 (the latter differing from the former by the factor $f_B f_{X_d}/f_{BH^+}$ which is not a constant) and a reaction obeying (3*b*) is therefore unlikely to obey (5*b*).

It therefore appears that the first assumption is the correct one and that the rearrangement (*f*) rather than the proton-transfer (*d*), (*e*) is the rate-determining step. Brönsted originally took the view that the proton-transfer is always rate-determining in acid catalysis, but evidence has since accumulated which shows that the other alternative applies in many instances (Euler, *Z. physikal. Chem.*, 1927, **131**, 107 and earlier papers; Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686) and this reaction is evidently one of them. It is hoped to adduce further evidence for this conclusion from the study of the effect of substituents on the rate of rearrangement. If the distinction between the linear variation of rate with oxonium-ion concentration or acidity function respectively can be further substantiated as a criterion of the rate-determining step, the concept of acidity function becomes one of the first importance in the study of the mechanisms of catalysed reactions.

It remains then to explain the variation of the ratio $[R{\cdot}OH_2^+]/[R{\cdot}OH]$ or of the acidity function, with medium composition, the log k–[EtOH] curve being identical with the log $[R{\cdot}OH_2^+]/[R{\cdot}OH]$)–[EtOH] curve according to equations (3*a*) and (3*b*). The linear decrease of k up to 80% alcohol content is undoubtedly a dielectric-constant effect. In the case of hydrochloric acid, even if complete *dissociation* takes place in purely aqueous solution, this no longer applies to alcoholic solutions. The existence of ion pairs in solutions of strong electrolytes has been demonstrated by optical as well as conductivity measurements (Falkenhagen, "Elektrolyte," Leipzig, 1932, p. 304; Kraus and Fuoss, *J. Amer. Chem. Soc.*, 1935, **55**, 21; Halban and Litmanovitsch, *Helv. Chim. Acta*, 1941, **24**, 41) and dissociation will become more incomplete with increasing alcohol content of the medium, with a corresponding decrease in the ability of the solution to transfer protons to R·OH. In the case of acetic acid the decrease in D runs parallel with a decrease in the extent of *ionisation*. The primary solvent effect, *i.e.*, the direct influence of the change in dielectric constant on the equilibrium constants of reaction (*d*), (*e*) and on the rate of reaction (*f*), is likely to be small, since all these three reactions are of the dipole-ion type (cf. Moelwyn-Hughes and Sherman, J., 1936, 101). At 85% alcohol content, the proportion of $EtOH_2^+$ as compared with H_3O^+ ions becomes appreciable and as $EtOH_2^+$ gives up its extra proton much more readily than H_3O^+ (the equilibrium constant of the reaction $EtOH_2^+ + H_2O \rightleftharpoons EtOH + H_3O^+$ is about 100) the ratio $[R{\cdot}OH_2^+]/[R{\cdot}OH]$ increases. The curve relating k and [EtOH] is therefore really the sum of two broken curves (Fig. 2), one (*a*, *b*, or *c*) representing the decrease in k with decreasing acidity function and dielectric constant, and the other (*d*) the increase in k with the increase in the ratio $[EtOH_2^+]/[H_3O^+]$. When a weak acid such as acetic acid is used as catalyst, the curve is steeper, but flattens out for high values of [EtOH] without a distinct minimum, because the decrease of acid ionisation with increasing alcohol content is very

much faster than the decrease in dissociation of the strong hydrochloric acid, and of the same order of magnitude as the rate of increase of ethoxonium-ion concentration even at high alcohol concentrations.

The only reaction for which a mechanism analogous to the present one has been postulated and which has been studied under comparable conditions, appears to be the hydrochloric acid-catalysed inversion of sucrose (Amis, *J. Amer. Chem. Soc.*, 1941, **63**, 2231). A decrease in rate with increasing alcohol content (up to 50%) of the medium is also found, which is much smaller in magnitude than in the present case and is erroneously attributed to the formation of $EtOH_2^+$ ions, which would, if anything, tend to increase the rate. Actually the concentration of $EtOH_2^+$ ions at the alcohol concentrations used is negligible (cf. Goldschmidt, *loc. cit.*), and it is probable that the reaction mechanism is much more complicated than $S + H^+ \rightleftharpoons SH^+ \longrightarrow$ products (cf. Leininger and Kilpatrick, *J. Amer. Chem. Soc.*, 1938, **59**, 2891).

(B) *The Variation of Energy of Activation with Medium Composition. The Calculation of Isodielectric Energies of Activation.*—The data relating to rate constants at different temperatures are collected in Tables II and III, where $E_{exp.}$ represents the experimental energy of activation calculated from the Arrhenius equation. It will be seen that $E_{exp.}$ varies with medium composition and catalyst in an irregular fashion to the extent of 6 kg.-cals. (the estimated maximum error in $E_{exp.}$ is $\pm 0{\cdot}3$ kg.-cal.).

It was pointed out in Part I that $E_{exp.}$ calculated from the overall temperature coefficient includes the temperature dependence of the catalyst strength. The latter will be made up mainly of two parts: (i) the purely thermodynamic temperature dependence of the catalyst equilibrium such as $HOAc \rightleftharpoons H^+ + OAc^-$, and (ii) the dependence of that equilibrium on the dielectric constant of the medium which, in turn, varies considerably with temperature. The latter effect, together with the dependence, if any, of the reaction itself on the dielectric constant, will make up the larger part of the " untrue " portion of the experimental energy of activation. We can write this

$$E_{[D]} = E_{exp.} + \Delta E_D \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

TABLE II.

k = first-order rate constant (in min.$^{-1}$); $k_{[D]}$ = isodielectric rate constant (in min.$^{-1}$); $E_{exp.}$ = experimental energy of activation (in kg.-cals.); $E_{[D]}$ = isodielectric energy of activation (in kg.-cals.). Catalyst = 0·1M-HCl.

Temp.	10^4k.	$E_{exp.}$	$10^4k_{[D]}$.	$E_{[D]}$ by (8).	m.	b.	$E_{[D]}$ by (9).
			Medium: 20% EtOH (by vol.).				
30°	6·25	23·2	6·25	30·9	0·044	0·365	30·5
40	21·0		30·3				
50	64·4		133				
60	220		652				
			Medium: 40% EtOH (by vol.).				
30	2·09	22·7	2·09	29·7	0·044	0·342	29·5
40	7·70		10·8				
50	22·0		43·4				
60	56·8		157				
			Medium: 60% EtOH (by vol.).				
30	0·583	25·7	0·583	31·4	0·044	0·286	31·4
40	2·22		2·95				
50	8·10		14·3				
60	28·1		65·8				
			Medium: 80% EtOH (by vol.).				
30	0·210	25·7	0·210	30·2	0·044	0·225	30·7
40	0·851		1·06				
50	3·19		4·95				
60	10·0		19·5				

TABLE III.

Catalyst.	Solvent (vol.-% EtOH).	$E_{exp.}$	m.	b.	ΔE_D by (9).	$E_{[D]}$ by (9).
0·1M-HCl	20	23·2	0·044	0·365	7·3	30·5
	40	22·7	0·044	0·342	6·8	29·5
	60	25·7	0·044	0·286	5·0	31·4
	80	25·7	0·044	0·225	4·5	30·2
0·4M-HCl	20	23·5	0·042	0·365	6·8	30·3
	40	25·1	0·042	0·342	6·4	31·5
	60	24·7	0·042	0·286	5·3	30·0
	80	27·5	0·042	0·225	4·2	31·7
1M-HCl	20	24·2	0·040	0·365	6·5	30·7
	40	24·7	0·040	0·342	6·1	30·8
	60	25·8	0·040	0·286	5·1	30·9
	80	26·5	0·040	0·225	4·0	30·5
	90	27·3	—	—	—	—
	100	22·5	—	—	—	—
0·2M-H_2SO_4	20	23·8 *	0·037	0·365	6·2	30·0
1M-H_3PO_4	20	21·6 *	0·053	0·365	8·9	30·5
1M-AcOH	20	22·2 *	0·061	0·365	10·1	32·3

* Values taken from Part I.

where $E_{[D]}$ represents the *isodielectric energy of activation, i.e.*, for a medium of constant dielectric constant. Actually, since D decreases with increasing temperature, $E_{exp.}$ will generally be smaller than $E_{[D]}$ for reactions exhibiting mainly specific ion catalysis, *i.e.*, ΔE_D will be positive.

The correction for ΔE_D can be applied by combining Wyman's data (*J. Amer. Chem. Soc.*, 1931, **53**, 3292) for the dielectric constants of ethyl alcohol–water mixtures at different temperatures with the data on the variation of the reaction rate with the dielectric constant referred to above. Wyman's data can be expressed with sufficient accuracy by

$$D = a - b(t - 20) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where a and b are constants for any one reaction medium and t is the temperature. By combining (1) and (7), the correction takes the simple form

$$k_{[D]} = k \text{ antilog } [(t_2 - t_1)mb] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

where $k_{[D]}$ represents the rate constant at the temperature t_2 for a medium having the same dielectric constant as at t_1 and will be subsequently referred to as *isodielectric rate constant.* Values of a and b are tabulated by Wyman, and values of m can be taken directly from Table I. The large magnitude of the correction is evident from the $k_{[D]}$ values given in Table II. $E_{[D]}$ is then obtained by applying the Arrhenius equation to the $k_{[D]}$ values.

There is a more direct way of obtaining $E_{[D]}$ in the present case, in view of the simple form of the relation between D and t. Since

$$E_{[D]} = 2{\cdot}3\boldsymbol{R}[T_1T_2/(T_2 - T_1)] \log k_{[D]2}/k_1$$

and, by (8)

$$\log k_{[D]2} = \log k_2 mb(T_2 - T_1)$$

hence

$$E_{[D]} = E_{exp.} + 2{\cdot}3\boldsymbol{R}T_1T_2mb \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

Table II shows the close agreement between values of $E_{[D]}$ obtained by (8) and by (9), an agreement which demonstrates the linearity of the $k_{[D]}$–$1/T$ plot. Equation (9) is, of course, the less accurate, but much more convenient to use. T_1 and T_2 are taken as the limits of the temperature range for which $E_{exp.}$ has been measured.

The objection may be raised that the dielectric constant of the actual solution and not that of the solvent should be used. This objection is answered if it is remembered that we are concerned with the variation in D and not its absolute value, and if the not unreasonable assumption may be made that variations in D of the solution are proportional to the variations in D of the solvent.

The method outlined above for determining isodielectric energies of activation is identical in principle with that employed by Svirbely and by Amis (*J. Amer. Chem. Soc.*, 1935, **57**, 1883; 1938, **60**, 330, 1613; 1941, **63**, 1606, 2231, 2621, 2833; *J. Physical Chem.*, 1943, **47**, 338). Both methods depend on the assumption that, within the range of medium composition considered, the chief influence of the change of solvent on the rate of reaction is exerted through the change in dielectric constant. This assumption appears to be strongly supported by the fact that while the values of $E_{exp.}$ vary in an irregular fashion with alcohol content and acid concentration over a range of 6 kg.-cals., the values of $E_{[D]}$ are constant to ± 1 kg.-cal. (Table III), a variation which does not greatly exceed the experimental error ($\pm 0{\cdot}3$ kg.-cal.) and would not in any case be unexpected, because, although the variation of D with temperature is assumed to be the chief factor responsible for the difference between the true and the experimental energy of activation, it is probably not the only factor. Variations of solvation and activities of the reactants with solvent composition have, of course, generally to be considered, but their influence in reactions of the present type is likely to be small, because the rate equation (3) involves the ratio of the activities of the actual reactant ($R{\cdot}OH_2^+$) and the very similar transition state.

The constancy of $E_{[D]}$ for media of different dielectric constants lends additional support to the reaction mechanism proposed in Part I and excludes a bi-ionic mechanism of the type $R{\cdot}OH \overset{\text{slow}}{\underset{\longleftarrow}{\longrightarrow}} R^+ + OH^- \xrightarrow{\text{fast}} R'{\cdot}OH$, the energy of activation of which should vary with the medium to an extent which can be calculated theoretically from electrostatic considerations (Moelwyn-Hughes and Sherman, *loc. cit.*; Amis, *loc. cit.*; Waters, J., 1942, 153).

The experimental procedure was as described in Part I. Solutions of hydrochloric acid in absolute alcohol were prepared by the method of Hickling and Salt (*Trans. Faraday Soc.*, 1941, **37**, 224).

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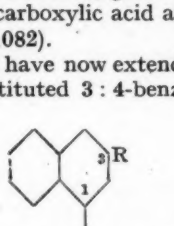
120. 3 : 4-*Benzfluorenones. Part I. The Effect of Groups on their Formation and their Fission with Alkali.*

By Fawzy Ghali Baddar and Munir Gindy.

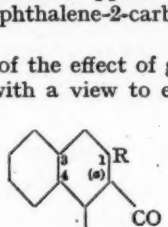
Cyclisation of 1-phenylnaphthalene-2′-carboxylic acids may give 3 : 4-benzfluorenones or *meso*benzanthrones, and it is found that the course of the reaction is greatly influenced by substituents. The direction of fission of 3 : 4-benzfluorenones by fused potassium hydroxide is also influenced by substituents in the molecule. This influence is attributed mainly to the polar character of the substituent.

It has been stated by Baddar (J., 1941, 310) that whereas 1-phenylnaphthalene-2′-carboxylic acid (I, R = H) and its 4-alkyl derivatives give on ring closure a mixture of a 3 : 4-benzfluorenone and a *meso*benzanthrone in the ratio of about 2 : 1 respectively, yet 1-phenylnaphthalene-2′ : 3-dicarboxylic acid gives *meso*benzanthrone-2-carboxylic acid (III; R = CO_2H) as the main product together with traces of 3 : 4-benzfluorenone-1-carboxylic acid (II). Baddar (*loc. cit.*) attributed this to the deactivation of carbon atom in position 2 (I) by the proximity of the carboxyl group. This deactivation is undoubtedly responsible also for the production of 1-phenylnaphthalene-2′ : 3-dicarboxylic acid and 3-benzoyl-1-phenylnaphthalene-2′-carboxylic acid by the alkaline fission of 3 : 4-benzfluorenone-1-carboxylic acid and 1-benzoyl-3 : 4-benzfluorenone respectively. 3 : 4-Benzfluorenone, however, gives on similar treatment, approximately an equimolecular mixture of 1-phenylnaphthalene-2′-carboxylic acid and 1-phenylnaphthalene-2-carboxylic acid (Schaarschmidt and Georgeacopol, *Ber.*, 1918, **51**, 1082).

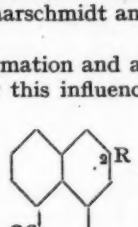
The authors have now extended the study of the effect of groups on the formation and alkaline fission of differently substituted 3 : 4-benzfluorenones, with a view to elucidate whether this influence is of polar or steric origin.



(I.)



(II.)



(III.)

1-*Methoxy*-3 : 4-*benzfluorenone and* 2-*Methoxy*mesobenzanthrone.—4-Iodo-2-naphthyl methyl ether was prepared in poor yield from 4-amino-2-naphthyl methyl ether (cf. Morgan and Evens, J., 1919, **115**, 1126), 2-hydroxy-1 : 4-naphthaquinone being one of many by-products (a better method is that of Hodgson and Birtwell, J., 1943, 468). This ether, on condensation with methyl *o*-iodobenzoate in presence of copper, gave 3-*methoxy*-1-*phenylnaphthalene*-2′-*carboxylic acid*, which afforded on ring closure a mixture of 1-*methoxy*-3 : 4-*benzfluorenone* (II; R = OMe, R_1 = H) and 2-methoxy*meso*benzanthrone (III; R = OMe). Although complete separation of the two constituents could not be effected owing to lack of material, yet the former was proved to be predominant.

3 : 4-*Benzfluorenone*-8-*carboxylic Acid* (II; R = H, R_1 = CO_2H).—1-Phenylnaphthalene-2′ : 3′-dicarboxylic acid, prepared by condensation of 1-iodonaphthalene with ethyl 3-iodophthalate, was converted into its *anhydride*, which gave on cyclisation a mixture of 3 : 4-*benzfluorenone*-8-*carboxylic acid* and *meso*benzanthrone-8-carboxylic acid, the latter predominating.

3 : 4-*Benzfluorenone*-7-*carboxylic Acid*.—1-Phenylnaphthalene-2 : 4′-dicarboxylic acid, prepared by the condensation of methyl 1-bromo-2-naphthoate with ethyl *p*-iodobenzoate, gave on ring closure 3 : 4-*benzfluorenone*-7-*carboxylic acid* only.

3 : 4-Benzfluorenone- and *meso*benzanthrone-carboxylic acids were characterised by decarboxylation to 3 : 4-benzfluorenone and *meso*benzanthrone, respectively.

Alkaline Fission of 3 : 4-*Benzfluorenones*.—3 : 4-Benzfluorenone-8-carboxylic acid gave on fission with alkali 1-*phenylnaphthalene*-2 : 3′-*dicarboxylic acid*. 3 : 4-Benzfluorenone-7-carboxylic acid, however, gave a mixture of acids from which 1-phenylnaphthalene-2 : 4′-dicarboxylic acid was isolated in a pure state. The fact that the remaining mixture of acids gave with warm concentrated sulphuric acid a brownish-red solution with a strong green fluorescence, characteristic of *meso*benzanthrones, indicates that the fission product most probably contains also 1-phenylnaphthalene-2′ : 4′-dicarboxylic acid, as this would be expected to accompany the formation of a *meso*benzanthrone.

From these results it appears that this deactivation effect cannot be attributed to ordinary steric hindrance, as this would necessitate preferential cleavage of the bond linking the carbonyl carbon atom and carbon atoms (*b*) and (*a*) (see II) in 3 : 4-benzfluorenone-1- and -8-carboxylic acids, respectively. Similarly, it would have resulted also in the formation of 2-methoxy*meso*benzanthrone as the main product on ring closure of 3-methoxy-1-phenylnaphthalene-2′-carboxylic acid, which is not the case (cf. the effect of *o*-substituents on the formation and hydrolysis of esters, chlorides, amides, and nitriles of benzoic acids; Lloyd and Sudborough, J., 1899, **75**, 580). The factors, therefore, which operate to determine the point of cleavage of 3 : 4-benzfluorenones, as well as the mode of cyclisation of 1-phenylnaphthalene-2′-carboxylic acids, are of polar origin (cf. Kutz and

Adkins, *J. Amer. Chem. Soc.*, 1930, **52**, 4036), depending to a great extent on the electron density at carbon atoms (*a*) and (*b*) in (II) and 2 and 2′ in (I) (cf. Lea and Robinson, J., 1926, 2351).

Experimental.

(M.p.'s are not corrected. Microanalyses were carried by Dr. G. Weiler and Dr. B. Strauss of Oxford.)

4-Nitro-2-naphthyl Methyl Ether.—The crude nitro-naphthol (5 g.) was methylated with 10% sodium hydroxide solution (40 c.c.) and methyl sulphate (8 c.c.); the precipitated ether crystallised from alcohol in yellow, lustrous plates, m. p. 102—103° (Morgan and Evens, *loc. cit.*, give m. p. 100—103°); yield, 60—70%.

4-Amino-2-naphthyl Methyl Ether Sulphate.—The powdered nitro-ether (10 g.) was dissolved in ether (1 l.), aluminium amalgam (8·6 g.) added, and the mixture left for 4 hours with frequent shaking. The fluorescent ethereal filtrate was dried, cooled in ice, and the base sulphate precipitated by addition of the calculated amount of concentrated sulphuric acid; yield about 90%. *4-Acetamido-2-naphthyl methyl ether*, prepared in benzene solution, crystallised from dilute alcohol in silky needles, m. p. 179° (Found: C, 73·0; H, 5·8; N, 6·4. $C_{13}H_{13}O_2N$ requires C, 72·5; H, 6·1; N, 6·5%).

4-Iodo-2-naphthyl Methyl Ether.—The base sulphate (17 g.) was dissolved in hot 2N-sulphuric acid (240 c.c.), quickly cooled, and a further 40 c.c. of concentrated sulphuric acid added. The mixture was thoroughly cooled to − 5°, and sodium nitrite solution (5·5 g. in 40 c.c. of water) slowly added with stirring. The diazo-solution was stirred for about 15 minutes, treated with powdered urea (2·8 g.), and slowly added to a solution of potassium iodide (23·4 g. in 130 c.c. of 2N-sulphuric acid). The solution was left overnight, then heated on the water-bath for 20 minutes. The precipitated semi-solid was extracted with benzene, washed with alkali to remove phenolic by-products, and then distilled in a vacuum; b. p. 200—210°/3 mm. The solidified yellow distillate gave on crystallisation from light petroleum (b. p. 30—50°) 4-iodo-2-naphthyl methyl ether in colourless plates, m. p. 66—67° (Hodgson and Birtwell, *loc. cit.*, give m. p. 67°) (Found: C, 47·0; H, 3·4; I, 45·7. Calc. for $C_{11}H_9OI$: C, 46·5; H, 3·2; I, 44·7%); yield, 15%. In an attempt to isolate the iodo-compound by steam-distillation, only a small fraction was volatile, and the phenolic residue dissolved in alkali to a red solution and melted after crystallisation from dilute methyl alcohol or benzene at 187—188°. On sublimation in a vacuum it gave orange yellow crystals, m. p. 191—192°, undepressed on admixture with a sample of 2-hydroxy-1 : 4-naphthaquinone (kindly supplied by Dr. Gabra Soliman), prepared by the action of cold alcoholic alkali on 2 : 4-dihydroxynaphthalene. Its formation may be due to the decomposition of the diazonium compound to 2 : 4-dihydroxynaphthalene which was then oxidised on being dissolved in alkali to 2-hydroxy-1 : 4-naphthaquinone.

3-Methoxy-1-phenylnaphthalene-2′-carboxylic Acid.—A mixture of 4-iodo-2-naphthyl methyl ether (0·5 g.) and methyl *o*-iodobenzoate (1·0 g.) was stirred at 180—190°. Copper bronze (0·5 g.) was then added during 30 minutes, the temperature being slowly raised to 200—210°, and the mixture was kept at this temperature for a further 4—5 hours, then worked up as usual (cf. Baddar and Warren, J., 1938, 401); the sticky solid obtained from the benzene extract was esterified with diazomethane and distilled in a vacuum, b. p. 200—210°/3 mm. The yellowish-brown distillate gave on hydrolysis *3-methoxy-1-phenylnaphthalene-2′-carboxylic acid*, which crystallised from methyl alcohol in long cubic rods, m. p. 191—192° (Found: C, 78·1; H, 5·1. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%); yield, 26%.

*1-Methoxy-3 : 4-benzfluorenone and 2-Methoxy*meso*benzanthrone.*—3-Methoxy-1-phenylnaphthalene-2′-carboxylic acid was dissolved in benzene and cyclised with phosphoric oxide (cf. Baddar, *loc. cit.*). On crystallisation from methyl alcohol, two types of crystals were obtained (yellow and orange), which were incompletely separated by mechanical means. Attempts to purify them by fractional crystallisation or chromatography failed. The yellow crystals were, however, proved to be 2-methoxy*meso*benzanthrone as they gave with concentrated sulphuric acid a yellowish-red solution with a green fluorescence, and on fusion with potassium hydroxide followed by reduction with sodium hyposulphite a blue-green vat was produced, which dyed cotton green, identical with that of Caledon jade-green, *i.e.*, 2 : 2′-dimethoxydibenzanthrone. The orange crystals were the major product and melted after several crystallisations from methyl alcohol at 148—150° (Found: C, 82·5; H, 4·5. $C_{18}H_{12}O_2$ requires C, 83·0; H, 4·7%). These were proved to be *1-methoxy-3 : 4-benzfluorenone*, probably contaminated with traces of 2-methoxy*meso*benzanthrone, by the following tests: (1) they gave with concentrated sulphuric acid a brownish-green solution; (2) when heated at 100° with concentrated sulphuric acid, they were easily sulphonated (*meso*benzanthrones, in general, are much more resistant to sulphonation than are 3 : 4-benzfluorenones); (3) on fusion with potassium hydroxide followed by reduction with sodium hyposulphite, only very little green vat was obtained.

Ethyl 3-Nitrophthalate.—This ester, prepared by refluxing a mixture of 3-nitrophthalic acid (60 g.), absolute alcohol (240 c.c.), and concentrated sulphuric acid (80 c.c.) for 8 hours on the water-bath, crystallised from light petroleum in long, colourless needles, m. p. 45—46°. Miller (*Annalen*, 1881, **208**, 243) and Curtius and Semper (*Ber.*, 1913, **46**, 1168) give m. p. 45° and 46° respectively.

Ethyl 3-p-Toluenesulphonamidophthalate.—This was prepared in the usual manner and crystallised from benzene–light petroleum (70—80°) in colourless needles, m. p. 147—148° (Found: N, 4·0; S, 8·8. $C_{19}H_{21}O_6NS$ requires N, 3·6; S, 8·2%). It is soluble in benzene, moderately soluble in water, and sparingly soluble in light petroleum.

1-Phenylnaphthalene-2′ : 3′-dicarboxylic Acid.—Ethyl 3-iodophthalate (2 g.) and 1-iodonaphthalene (1·6 g.) were heated together with stirring in a boiling nitrobenzene bath; copper bronze (2·0 g.) was slowly added during ½ hour, and the heating continued for 4 hours. The product was hydrolysed with alcoholic sodium hydroxide and the sodium salt of the acids dissolved in water (80—90 c.c.) and extracted with benzene to remove neutral substances. The alkaline solution (charcoal) gave on acidification a white amorphous precipitate which crystallised from alcohol–benzene to give 1-phenylnaphthalene-2′ : 3′-dicarboxylic acid in colourless cubic crystals (yield, 36%), m. p. 192—193° (quick heating); when slowly heated it melted at 178—179°, probably owing to anhydride formation (see below). The acid was, therefore, best identified as its *methyl* ester, which crystallised from alcohol in colourless crystals, m. p. 133—134° (Found: C, 74·8; H, 5·3. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%).

1-Phenylnaphthalene-2′ : 3′-dicarboxylic Anhydride.—The acid (1 part) was refluxed with acetic anhydride (3 parts) for ½ hour. The *anhydride* was then precipitated by addition of ether, and crystallised from benzene–light petroleum (b. p. 60—80°) in colourless leaflets, m. p. 179—180° (Found: C, 79·0; H, 3·6. $C_{18}H_{10}O_3$ requires C, 78·8; H, 3·7%); yield, 85%.

3 : 4-Benzfluorenone-8-carboxylic Acid and meso*Benzanthrone-8-carboxylic Acid.*—1-Phenylnaphthalene-2′ : 3′-dicarboxylic anhydride (2 g.), carbon disulphide (15 c.c.), and finely powdered aluminium chloride (3 g.) were refluxed on the water-bath for 4 hours with occasional shaking. Carbon disulphide was evaporated off, and the product decomposed with dilute hydrochloric acid. The acids were filtered off, dissolved in hot ammonium hydroxide, the solution filtered, and the acids reprecipitated. The dry product was washed with a little ether, then crystallised from glacial acetic acid; the silky brown-red needles precipitated at once were proved to be *3 : 4-benzfluorenone-8-carboxylic acid* (0·4 g.), m. p. 276—276·5°, as they gave 3 : 4-benzfluorenone on decarboxylation with copper bronze and quinoline (Found: C, 78·8; H, 3·6. $C_{18}H_{10}O_3$ requires C, 78·8; H, 3·7%). The yellow needles (0·8 g.) precipitated on standing were proved to be *meso*benzanthrone-8-carboxylic acid, m. p. 262—263°, as they gave on decarboxylation *meso*benzanthrone (Found:

C, 78·6; H, 3·7. Calc. for $C_{18}H_{10}O_3$: C, 78·8; H, 3·7%); Copp and Simonsen (J., 1942, 212) give m. p. 254—255°. The acetic acid mother-liquor gave on concentration a mixture of the two acids, *meso*benzanthrone-8-carboxylic acid predominating. Methyl *meso*benzanthrone-8-carboxylate was prepared by means of diazomethane in dioxan as brilliant yellow needles, m. p. 173·5—174·5°, undepressed on admixture with an authentic specimen (kindly supplied by Prof. J. L. Simonsen). The acid prepared by hydrolysing the ester with acetic–hydrochloric acids melted at 257—258°. This may account for the low m. p. of the acid prepared by Copp and Simonsen (*loc. cit.*), which they obtained by hydrolysis of its methyl ester.

Fusion of 3 : 4-*Benzfluorenone*-8-*carboxylic Acid with Potassium Hydroxide.*—The benzfluorenone (1 part) was added during 10 minutes to fused potassium hydroxide (7 parts) at 200—210°, the temperature being slowly raised to 225—230° and kept thereat with frequent stirring for a further ½ hour. The alkaline fluorescent solution was filtered and acidified. The dry acid, which was soluble in benzene, became insoluble on being digested with successive small amounts of benzene, probably owing to dehydration. This process was repeated until no more acid was precipitated. On crystallisation from alcohol–benzene, then from dilute alcohol, 1-*phenylnaphthalene*-2 : 3′-*dicarboxylic acid* was obtained in colourless crystals, m. p. 255—256°, mixed m. p. with 1-phenylnaphthalene-2′ : 3′-dicarboxylic acid 180—210° (Found: C, 74·0; H, 4·2. $C_{18}H_{12}O_4$ requires C, 74·0; H, 4·1%). When warmed with concentrated sulphuric acid it gave a green non-fluorescent solution.

1-*Phenylnaphthalene*-2 : 4′-*dicarboxylic Acid.*—A mixture of methyl *p*-iodobenzoate (2 g.) and methyl 1-bromo-2-naphthoate (2 g.) was thoroughly dried and stirred in an ethyl cinnamate bath at 200—210°. Copper bronze (2 g.) was added during 30 minutes, and the mixture slowly (½ hour) heated to 240—250°, kept thereat for 2 hours, again slowly (½ hour) heated to 260—265°, and stirring continued for a further 3—4 hours. The product was extracted with acetone, and removal of the solvent gave a viscous brown oil, which was twice extracted with hot alcohol (total 120—150 c.c.). The cold alcoholic extract was filtered from the tarry residue (about 0·1 g.), concentrated to about 30 c.c., then hydrolysed with alcoholic sodium hydroxide, filtered off, and worked up as usual. The dry acids were extracted with hot benzene (residue *ca.* 0·15—0·2 g.), the extract concentrated to about 20 c.c., then kept for two days and filtered from the precipitated acids (0·15—0·2 g.), probably 1 : 1′-dinaphthyl-2 : 2′-dicarboxylic acid mixed with traces of 1-phenylnaphthalene-2 : 4′-dicarboxylic acid. Removal of the benzene gave a sticky solid which was heated at 160° and the crystalline white sublimate, m. p. 220—225°, rejected. The dark brown acid residue was then esterified with diazomethane in ether and fractionally distilled at 3 mm. The first fraction, b. p. 150—180°, crystallised from light petroleum in colourless crystals, m. p. 70—72°, and was not investigated. The second fraction, b. p. 200—240°, failed to crystallise and was therefore directly hydrolysed. The precipitated acids were filtered off, dried, and extracted with benzene, the benzene evaporated, and the process repeated until the acids became insoluble in benzene. The crude product was fractionally crystallised from dilute acetic acid (*ca.* 30%). The first crop, m. p. 255—260°, was recrystallised from dilute acetic acid to give 1-*phenylnaphthalene*-2 : 4′-*dicarboxylic acid* in colourless rods, m. p. 265—266° (Found: C, 73·7; H, 4·2. $C_{18}H_{12}O_4$ requires C, 74·0; H, 4·1%). The second crop melted at 220—235° and was proved to be an inseparable mixture of 1-phenylnaphthalene-2 : 4′- and 1 : 1′-dinaphthyl-2 : 2′-dicarboxylic acids, for it gave on cyclisation a mixture of 3 : 4-benzfluorenone-7-carboxylic acid and an anthanthrone; yield, *ca.* 7%.

3 : 4-*Benzfluorenone*-7-*carboxylic Acid.*—1-Phenylnaphthalene-2 : 4′-dicarboxylic acid chloride was treated with aluminium chloride in carbon disulphide and worked up as usual (cf. Schaarschmidt, *Ber.*, 1917, **50**, 294). The resulting acid chloride was refluxed with 15% potassium hydroxide solution for ½ hour, the solution filtered and acidified, and the crystals filtered off. On crystallisation from nitrobenzene, 3 : 4-*benzfluorenone*-7-*carboxylic acid* separated in lustrous, orange-red crystals, m. p. 323—324° (Found: C, 78·7; H, 3·8. $C_{18}H_{10}O_3$ requires C, 78·8; H, 3·7%). It gave on decarboxylation 3 : 4-benzfluorenone.

Fusion of 3 : 4-*Benzfluorenone*-7-*carboxylic Acid with Potassium Hydroxide.*—The acid (0·1 g.) was fused with potassium hydroxide as for the 8-carboxylic acid. The product obtained after refluxing with benzene (0·05—0·06 g.) was a mixture, m. p. 225—235°; it was extracted with dilute alcohol (20 c.c., 12%) and filtered hot. The insoluble fraction melted at 250—255° and gave on crystallisation from dilute acetic acid 1-phenylnaphthalene-2 : 4′-dicarboxylic acid in cubic rods, m. p. 263—264° (0·02 g.; *ca.* 40%), undepressed on admixture with an authentic specimen. The alcoholic mother-liquor was evaporated to dryness, and the residue (0·03—0·04 g.), m. p. 220—230°, was most probably a mixture of 1-phenylnaphthalene-2 : 4′- and -2′ : 4′-dicarboxylic acids. Their separation could not be effected either by fractional crystallisation or by refluxing with acetic anhydride followed by differential decomposition of their mixed anhydrides with sodium carbonate or hydroxide solution (cf. Huntress and Seikel, *J. Amer. Chem. Soc.*, 1939, **61**, 1358).

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121. *The Asymmetric Photolysis of β-Chloro-β-nitroso-αδ-diphenylbutane with Circularly Polarised Light.*

By STOTHERD MITCHELL and IAN M. DAWSON.

Some years ago, the successful asymmetric photolysis of humulene nitrosite was described (Mitchell, J., 1930, 1829), but attempts to extend this work to simpler nitrosites and ψ-nitroles did not lead to positive results. Recently, however, chloronitroso-compounds were found to be more suitable, and experiments have now been carried out with β-chloro-β-nitroso-αδ-diphenylbutane. This compound (in methyl alcohol) was irradiated with right-handed circularly polarised red light until about 90% of it had been decomposed. The unattacked portion was recovered and showed $a^{20°}_{5300} = -0·10°$ ($l = 1$, $c = 4\%$ in methyl alcohol). A corresponding experiment with left-handed light gave the value +0·11°.

IN 1896, Cotton found that certain optically active substances absorb right- and left-handed circularly polarised light to different extents and he called the phenomenon "circular dichroism." He suggested that, if a substance possessed this property when in the dextro- or lævo-form and was susceptible to photochemical decomposition, it might be possible to effect a partial resolution of the racemic form by irradiating it with one type of circularly polarised light. This problem of asymmetric photolysis is of interest in connection with the question of the origin of optically active compounds in Nature, but its experimental realisation is extremely difficult (see Mitchell, "The Cotton Effect," London, 1933; Mathieu, "La Synthèse Asymétrique," Paris, 1935). In the first place, although many substances have been found to exhibit circular dichroism, the relative difference in

absorption of the two kinds of circularly polarised light is usually only a few units %. It is expressed as the "anisotropy factor," $(\varepsilon_l - \varepsilon_r)/\varepsilon$, where ε_r, ε_l, and ε are the molecular extinction coefficients for right- and left-handed and ordinary light, respectively. In addition, there are three photochemical requirements: (*a*) destruction of the molecular dissymmetry by the light, (*b*) a quantum efficiency of 1, and (*c*) absence of dark reactions. Of these (*a*) is essential, and (*b*) and (*c*) should be fulfilled as strictly as possible.

Despite many attempts at asymmetric photolysis by a number of workers, conclusive results were not obtained till 1930, when Kuhn and Knopf (*Z. physikal. Chem.*, *B*, **7**, 292) decomposed the dimethylamide of α-azidopropionic acid with circularly polarised ultra-violet light, and Mitchell (J., 1930, 1829) acted on humulene nitrosite with circularly polarised red light. It was thought desirable to extend the work to simpler nitroso-compounds, although it was realised that they might not yield such striking results.

The nitrosites of bornylene, phellandrene, and zingiberene were first studied by Mitchell and Cormack (J., 1932, 415). They were white solids which gave colourless solutions in organic solvents at room temperature. A solution of bornylene nitrosite (in toluene) turned blue on warming (due to dissociation of double molecules) but lost its colour again on cooling. The blue solution showed circular dichroism and at 70° had an anisotropy factor of about 0·04. Unfortunately, considerable decomposition was caused by the prolonged heating which would have been necessary for photochemical experiments, and, as the phellandrene and zingiberene compounds were even less stable, work upon these three nitrosites was abandoned.

Some ψ-nitroles, $CR(NO_2)NO{\cdot}R'$, were next examined. Although usually white in the solid state, they dissolve in organic solvents to give blue solutions at room temperature, which absorb oxygen in red light to afford the corresponding dinitro-compounds. Hammick and Lister (J., 1937, 489) found the quantum efficiency of this reaction for dimethyl-ψ-nitrole in benzene solution to be 0·89. When R and R′ are different, the molecule has an asymmetric carbon atom which is destroyed by the photo-oxidation. An attempt was made (with Roy R. Gordon) to prepare the active form of methylethyl-ψ-nitrole from *d*-β-nitrobutane (cf. Kuhn and Albrecht, *Ber.*, 1927, **60**, 1297), but our product had no rotation. We also studied the photo-oxidation of methylethyl-ψ-nitrole, but found that it was accompanied by an appreciable dark reaction. With ψ-nitroles of higher molecular weight the dark reaction became more rapid, so work on these compounds was abandoned.

An investigation of the photochemical action of nitrosyl chloride on *n*-hexane (Mitchell and Carson, J., 1936, 1005) directed attention to chloronitroso-compounds, and the photolysis of β-chloro-β-nitrosobutane was carried out by Mitchell and Cameron (J., 1938, 1964). It appeared from this work that chloronitroso-compounds would be suitable for asymmetric photochemical experiments, but this one was rather volatile. Before proceeding further, however, it was desirable to find if the chlorine atom interferes with the Cotton effect of the nitroso-group in this type of compound. Satisfactory evidence on this point was obtained by Mitchell and Simpson (J., 1940, 784) from a study of *l*-menthyl *d*-chloro-β-nitrosobutyrate. It had an anisotropy factor of about 0·04 (in ethyl alcohol) and analysis of the rotatory dispersion curve showed that the contribution due to the nitroso-group was not affected by the presence of the chlorine atom.

β-Chloro-β-nitroso-αδ-diphenylbutane, $CH_2Ph{\cdot}CCl(NO){\cdot}CH_2{\cdot}CH_2Ph$, was selected for further work from a number of compounds examined by Mitchell, Schwarzwald, and Simpson (J., 1941, 602). It fulfilled the three photochemical requirements outlined above: (*a*) The main product of photolysis (in methyl alcohol) was the hydrochloride of αδ-diphenylbutan-β-oneoxime, so the asymmetry of the carbon atom was destroyed by the light. (*b*) The quantum efficiencies for λ 6100 and 6580 A. were 1·10 and 0·78, respectively, giving an average value of 0·94. (*c*) There was no dark reaction.

Preliminary asymmetric photochemical experiments, in which the compound was decomposed to the extent of 75%, showed conclusively that irradiation with right-handed light produced negative rotation for λ 5300 A., a wave-length on the short-wave side of the absorption band ($\varepsilon_{max.}$ = 6580 A.), and positive rotation (for the same wave-length) was developed with left-handed light. The rotations observed were rather small, however, and in order to obtain larger values we decided to continue the irradiation till about 90% of the chloronitroso-compound had been decomposed. As it was difficult to isolate the unchanged substance in a pure condition if the decomposition had gone too far, we carried out the asymmetric photolysis in four stages (one of 50% and three of 40%), recovering the unattacked compound after each stage. This procedure also saved a considerable amount of light. Polarimetric examination of the final specimens which had been exposed to right- and left-handed light, respectively, gave the values $\alpha^{20°}_{5300} = -0{\cdot}10°$ and $+0{\cdot}11°$ ($l = 1$, $c = 4\%$, in methyl alcohol), or $[\alpha]^{20°}_{5300} = -2{\cdot}50°$ and $+2{\cdot}75°$.

Experimental.

αδ-Diphenylbutan-β-one.—This was prepared at first by oxidation of β-hydroxy-αδ-diphenylbutane (from β-phenylethylmagnesium chloride and phenylacetaldehyde; cf. Tiffeneau, Orékhoff, and Lévy, *Bull. Soc. chim.*, 1931, **49**, 1846), but owing to difficulty in obtaining phenylacetaldehyde, the method described by Haworth, Mavin, and Sheldrick (J., 1934, 1424) was also used. Phenylacetonitrile was condensed with methyl β-phenylpropionate (cf. Beckh, *Ber.*, 1898, **31**, 3160) to give α-cyano-αδ-diphenylbutan-β-one, which was converted into the corresponding amide and then into the required ketone (m. p. 43°).

αδ-Diphenylbutan-β-oneoxime.—When αδ-diphenylbutan-β-one is treated with hydroxylamine hydrochloride and potassium acetate in aqueous alcohol and only slight heat is applied, a mixture of the two forms of the oxime is obtained in which the high-melting form (m. p. 121°) predominates. Prolonged heating (over 3 hours) favours the production of the low-melting form (m. p. 80°). For the present purpose it was not necessary to separate the two forms.

β-Chloro-β-nitroso-αδ-diphenylbutane.—This is best prepared by passing chlorine into a solution of αδ-diphenylbutan-β-oneoxime in dry ether until the oxime hydrochloride, which is precipitated at first, has disappeared and the solution is green. The ether is then distilled off, and the product crystallised from methyl alcohol; m. p. 47°. It can also

be prepared directly from the oxime hydrochloride (recovered from photolysis) but it is more satisfactory to use the oxime (which crystallises out when the hydrochloride is boiled with methyl alcohol and the solution allowed to cool).

Apparatus.—The light source was an automatic carbon arc run from a D.C. generator with a current of 10 amps. A condensing lens ($f = 3''$) formed an enlarged image of the positive pole on a projection lens ($f = 12''$) about 2 feet away. Immediately behind the condenser was a diaphragm with a square aperture of 2 in. side. Following this was a 3-inch circulating water filter and a red glass filter for cutting off infra-red rays and light below 6000 A., respectively. In front of the projection lens a large double-image prism and a $\lambda/4$ plate (for red light) were fixed. Two images of the square aperture were thus produced side by side, and each was received on a glass cell ($5 \times 5 \times 2$ cm.), the $\lambda/4$ plate being oriented so that one cell was illuminated with right-handed and the other with left-handed circularly polarised light.

Procedure.—5 G. of β-chloro-β-nitroso-αδ-diphenylbutane were weighed into each cell, and a piece of plate glass through which a small hole had been drilled was cemented on top of each. When the cement had set, the cells were filled with methyl alcohol (freed as far as possible from dissolved oxygen) and the holes were closed with ground stoppers made from pieces of capillary tubing fitted with stopcocks. Some of the blue solid did not dissolve at first, but it gradually passed into solution as the experiment progressed. The cells were placed in position and irradiated until 50% decomposition had taken place (12 hours). This was determined by means of a photoelectric colorimeter. The contents of each cell were then evaporated to dryness under reduced pressure, and the blue compound was extracted from the oxime hydrochloride with dry ether. After removal of the ether, the residue was crystallised from methyl alcohol. The experiment was repeated four times, and the recovered chloronitroso-compound was used for the second stage of the asymmetric photolysis (40%) which was carried out twice. Only one experiment was necessary at the third and the fourth stage (each 40%). The average amount of chloronitroso-compound recovered from each cell in the four stages was 2·2, 2·1, 1·9, and 0·8 g., respectively. Approximately the same weights of oxime hydrochloride were also obtained. The total time of irradiation was 80 hours. The rotation measurements were made visually with a Hilger polarimeter (Lippich half-shadow angle = 5°) used in conjunction with a Zeiss–Winkel monochromator, the light source being a 100-c.p. Pointolite lamp.

We thank the Director of the Royal Institution for the loan of the large double-image prism which greatly increased the efficiency of our illuminating system.

UNIVERSITY OF GLASGOW. [*Received, February* 14*th*, 1944.]

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122. *Some New Ethyl and Phenyl Silicon Fluorides.*

By H. J. EMELÉUS and C. J. WILKINS.

Ethyl- and phenyl-substituted silicon fluorides of the types $SiRF_3$ and SiR_2F_2 have been prepared, thereby completing the series of ethyl and phenyl derivatives of silicon tetrafluoride. The new compounds are obtained in high yield from the corresponding chlorides by the action of zinc fluoride, and they are also produced by the action of hydrogen fluoride on the oxy-compounds.

The resistance of the compounds to hydrolysis rises rapidly with increase in the number of organic groups.

COMPARATIVELY few organo-substituted fluorides of non-metals are known, the majority having been prepared either by the action of hydrogen fluoride on the appropriate oxide or from the simple fluoride by substitution. Only trisubstituted silicon fluorides have been described; triethylfluorosilane has been prepared by both of the above methods (Flood, *J. Amer. Chem. Soc.*, 1933, **54**, 1735; Gierut, Sowa, and Nieuland, *ibid.*, 1936, **58**, 897), and the triphenyl and the tribenzyl derivative by the second method (Medox and Kotelkov, *J. Gen. Chem. U.S.S.R.*, 1937, **7**, 2007; Medox, *ibid.*, 1938, **8**, 291). We now describe the *mono-* and *di-ethyl-* and *-phenyl-silicon fluorides*, the completion of the series $SiEt_nF_{4-n}$ and $SiPh_nF_{4-n}$ providing information for a group study.

These compounds are readily prepared in high yield from the chlorides by conventional procedure, there being no evidence of disruption of the Si–C bond during the reaction. They are also formed by reaction of hydrogen fluoride (generated in the reaction mixture) with the appropriate siliconic acids, $(R{\cdot}SiO_2H)_x$, or silicones, $(SiR_2O)_x$; yields differ widely, but this alternative procedure provided confirmation of purity and identity of the products.

The reactivity of the compounds towards hydrolysing agents falls sharply as the number of organic groups increases, the behaviour of the series being as follows :

$SiEtF_3$ Immediately hydrolysed by water; reaction probably incomplete.
$SiPhF_3$ Immediately hydrolysed by water; reaction incomplete.
$SiEt_2F_2$, $SiPh_2F_2$ } Very slight hydrolysis with water, but rapid decomposition with alkalis.
$SiEt_3F$ High resistance to hydrolysis; undecomposed by sodium in liquid ammonia (Gierut, Sowa, and Nieuland, *loc. cit.*).
$SiPh_3F$ High resistance to hydrolysis (Medox and Kotelkov, *loc. cit.*).

Such behaviour could not entirely be ascribed to steric factors, for the effect in the chloride series is much less pronounced. Substituted germanium halides and analogous aliphatic types show a broadly parallel trend.

There is a regular decrement in boiling point, of 34° per halogen atom, on passing from ethylchlorosilanes to ethylfluorosilanes : the difference is somewhat lower in the phenyl series. Phenyltrifluorosilane and diphenyldifluorosilane (b. p.'s 101·8°, 252°) are both slightly more volatile than their carbon analogues (b. p.'s 102·4°, and 260°, decomp.).

EXPERIMENTAL.

The required silicon chlorides were prepared by interaction of Grignard reagents with silicon tetrachloride as described by Kipping and his colleagues. Oxy-compounds were obtained by hydrolysis of the chlorides, no attempt being made to

secure them in any particular degree of hydration. Ethylsiliconic acid separated when ethyltrichlorosilane was stirred into cold water; it was washed under running water, dried overnight at 120°, and finely powdered. Phenylsiliconic acid, prepared similarly, was dried for 2½ hours at 150°. Diethylsilicone was obtained by decomposing the dichloride with aqueous sodium hydrogen carbonate; it separated as a clear yellow oil and was used directly.

Ethyltrichlorosilane and diethyldichlorosilane are converted into the corresponding fluoro-compounds by the fluorides of zinc, lead, and antimony, but the first is best for preparative purposes because the action of antimony trifluoride is too vigorous and that of lead fluoride too sluggish. For the conversion of the phenylchloro- into the phenylfluoro-silanes zinc and antimony fluorides are equally useful.

Metallic fluorides used were of reagent quality, dried at 120—130°.

Preparation and Properties of Ethyltrifluorosilane.—(1) Ethyltrichlorosilane (b. p. 98—99°) was dropped from a tap funnel on to zinc fluoride maintained at 55° in a flask which had been swept out with dry nitrogen. The gaseous product was passed through a water-cooled reflux condenser into a liquid-air trap attached to a vacuum fractionation system. The condensate, a snow-white solid melting to a sparkling liquid, was volatile in the vacuum line at −79° and almost completely retained by a trap at − 111°. Further fractionation narrowed the limits of the cut to −87° and −108°. The yield of tensimetrically pure product was 60% (0·2531 G. of the gas occupied 226·0 c.c. at 179 mm. and 18·0°, corresponding to *M*, 113·5. $C_2H_5SiF_3$ requires *M*, 114·1). The fluorine content of the *silane*, determined by titration of strong acid liberated on hydrolysis, was 49·95% (Calc.: 50·0%).

Vapour pressure values for ethyltrifluorosilane were as follows:

Temp.	−71·5°	−68·3°	−62·7°	−55·9°	−47·3°	−43·4°
V. p. (mm.)	15	20	30	48·5	84·5	107
Temp.	−34·1°	−26·9°	−18·0°	−10·3°	−7·5°	−5·2°
V. p. (mm.)	183	263·5	410	576	650	725

The vapour pressure reaches 760 mm. at −4·4°, and the latent heat of vaporisation is 6181 cals./mol.

Gaseous ethyltrifluorosilane has a pungent smell and irritates the nose and throat intensely. It is readily inflammable, burning with a bright green-edged flame and forming a mist of silica. Hydrolysis with water is instantaneous, though the gas persists for a short time in moist air. The m. p. is −105° (pentane thermometer).

(2) A mixture of 12 g. of ethylsiliconic acid with 8 g. of calcium fluoride was gently warmed with 25 c.c. of concentrated sulphuric acid, so as to maintain a steady evolution of gas, the temperature being eventually raised to 120°. The gas was freed from hydrogen fluoride by passage through a solution of ethylsiliconic acid in sulphuric acid. It was collected in a liquid-air trap, and consisted of ethyltrifluorosilane (yield 25%) with a little silicon tetrafluoride, which was readily removed. Vapour-pressure values and the m. p. of the product were identical with those given in (1).

Preparation and Properties of Diethyldifluorosilane.—(1) Diethyldichlorosilane (b. p. 125—131°) was warmed to 60° with a 50% excess of zinc fluoride until reaction set in. The product (b. p. 60—61°) was removed through a fractionating column and purified by distillation in the vacuum line. The final cut lay between the limits −54° and −75°. Measurement of vapour density gave *M*, 123·6 [$(C_2H_5)_2SiF_2$ requires *M*, 124·1]. For analysis, the compound was absorbed in 2N-alkali, the solution diluted to 200 c.c. and faintly acidified with acetic acid, and the fluorine precipitated as calcium fluoride. The diethylsilicone remained in solution and did not interfere (Found: F, 29·9. $C_4H_{10}SiF_2$ requires F, 30·6%).

Vapour-pressure measurements by the static method gave the following values:

Temp.	−28·9°	−15·8°	−5·9°	+6·7°	+11·5°	23·4°	31·7°
V. p. (mm.)	9·5	25	41·5	80·5	103	189	263·5
Temp.	38·4°	45·6°	49·7°	55·0°	59·7°	60·9°	
V. p. (mm.)	345	450	521	625	726	760	

The latent heat of vaporisation is 7623 cals./mol.

Diethyldifluorosilane is a sparkling liquid with a faint smell reminiscent of that of oil of wintergreen. When added to water it sinks in oily drops, and only after 12 hours' standing does a thin film of hydrolysis products appear at the liquid interface. Alkaline reagents bring about very rapid hydrolysis. The compound does not attack glass at temperatures below its b. p. The m. p. is −78·7° ± 0·2°.

(2) 20 G. of the silicone were dissolved in 150 c.c. of concentrated sulphuric acid in a Pyrex flask, and 15 g. of calcium fluoride added. The flask was connected through liquid-air traps to the vacuum line. On gentle warming, a reaction set in and a layer of clear liquid soon accumulated on the surface of the reaction mixture. This liquid was distilled off and freed from silicon tetrafluoride by pumping at −70°. There were obtained 10 c.c. of product having b. p. 61—62° and m. p. −78°, in agreement with the values for diethyldifluorosilane (Found, acidimetrically: F, 30·4%).

Preparation and Properties of Phenyltrifluorosilane.—Chlorine was replaced by fluorine by means of zinc fluoride (50% excess) in a Kon-type flask. When once the reaction had been started by warming to about 60°, little further heating was necessary, the heat of the reaction distilling off the greater part of the lower-boiling product. This was twice redistilled from fresh zinc fluoride and then had b. p. 101·5°, the entire sample passing over within a range of 0·2°; yield 70%. Handled in contact with air, the substance attacks glass, but vacuum fractionation reduces the attack considerably. When kept in glass, it slowly formed a very involatile liquid, probably owing to action upon the glass. This made it always necessary to work with freshly distilled material.

Analysis was carried out by decomposing an alcoholic solution of the compound with excess of standard alkali and back-titrating the excess, litmus beng used as indicator (Found: F, 34·8; *M*, cryoscopic in benzene, 164·0, 168·7. $C_6H_5SiF_3$ requires F, 35·2%; *M*, 162·1). Attempts to determine the fluorine by precipitation as calcium fluoride gave low and erratic results. This was attributable to the fact that when the solution obtained by absorbing the substance in alkali was slightly acidified to promote complete precipitation of interfering phenylsiliconic acid, hydrolytic decomposition was reversed and re-formed phenyltrifluorosilane was lost through volatilisation.

Vapour-pressure values, determined statically below, and dynamically above, room temperature gave the b. p. as 101·8°/760 mm. and *L* as 8750 cals./mol. Data were as follows:

Temp.	−9·2°	+1·4°	+16·5°	35·8°	55·2°	72·2°	84·2°	92·1°	94·5°
V. p. (mm.)	6	10	24	60	147	279·5	428	557	619

Phenyltrifluorosilane is a colourless, inflammable liquid ($d_4^{17°}$ 1·212) with a pungent and aggressive smell. It is quickly hydrolysed by water and alkalis, and in the air the smell of the compound soon gives way to that of hydrogen fluoride.

An attempt was made to isolate derivatives of phenyltrichlorosilane, in which only one or two atoms of chlorine had been replaced by fluorine. Powdered antimony trifluoride was added in quantities of about 2 g. to a large excess (50 g.) of the liquid. After each addition the mixture was carefully warmed to about 50° to initiate the reaction. When the reaction had ceased, the lower-boiling material which might have been expected to contain fluorochlorides was distilled

off. The process was repeated several times and the total product carefully fractionated, but no indication of the presence of compounds of intermediate volatility was found.

Action of Hydrogen Fluoride on Phenylsiliconic Acid.—The reaction mixture, containing 21 g. of this acid, 25 g. of calcium fluoride, and 150 c.c. of concentrated sulphuric acid, was heated to 100° for 15 minutes, whereupon the volatile products were pumped off at about 5 mm., through a tube charged with equal parts of phenylsiliconic acid and phosphoric oxide, into a liquid-air trap. Small quantities of liquid and much silicon tetrafluoride were collected. Repetition of this procedure gave, in all, about 2 c.c. of liquid. This was fractionated in the vacuum line between −30° and −60°, but even when freshly distilled it always appeared somewhat milky. The b. p. under atmospheric pressure was 99—103°. The material was completely free from chloride, but the fluorine content was 31·4% (Calc.: 35·2%), pointing to the presence of impurity. The low yield may have been due to sulphonation, or to oxidation of the Ph–Si bond by the sulphuric acid.

Preparation and Properties of Diphenyldifluorosilane.—This compound was also prepared by interaction of zinc fluoride with the corresponding chloride (b. p. 200—202°/45 mm.). The crude product, b. p. 156—160°/50 mm., was purified by two further distillations under reduced pressure. There was finally obtained a liquid passing over at 158° at 50 mm.; yield 55% [Found: F, 17·1; *M*, cryoscopic in benzene, 207·7, 210·1. $(C_6H_5)_2SiF_2$ requires F, 17·3%; *M*, 220·1]. It was particularly important that the diphenyldichlorosilane used should be free from diphenyl, as this impurity is of closely similar volatility to the fluorinated product.

Vapour pressures were as follows:

Temp.	119·4°	149·8°	169·3°	188·3°	194·5°	216·5°	236·6°	242·8°
V. p. (mm.)	12·5	36·5	73	138	163	313	515	603

The accuracy of the temperature measurement at higher temperatures is believed to be ± 0·4°. The equation $\log p = 8{\cdot}288 - 2839/T$ defines the vapour-pressure curve, from which the normal b. p. is calculated to be 252·0°.

Diphenyldifluorosilane is a colourless and rather viscous oil ($d_4^{17°}$ 1·145) with a faint smell resembling that of anisole. It is not hydrolysed in moist air, and even in contact with water only a trace of hydrolysis product appears after a day or two, but ammonia and alkalis decompose it in a few seconds. The compound attacks glass slightly in the vicinity of the b. p.

IMPERIAL COLLEGE, LONDON, S.W. 7. [*Received, October 7th*, 1943.]

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123. *The Preparation, Resolution, and Optical Properties of* 2-*Amino*-n-*octane.*

By FREDERICK G. MANN and J. W. GEOFFREY PORTER.

The preparation and optical resolution of 2-amino-*n*-octane have been critically examined. Apart from the original purpose of this examination, the amine is of interest for two reasons: (*a*) its ready resolution provides an optically active amine of great value as a stereochemical reagent, (*b*) its optical properties present some striking features. The hydrochloride of the amine is freely soluble in a variety of solvents, both ionising and non-ionising; in the latter type of solvent it is apparently uniformly associated. These properties are connected with the "acid-effect" which the amine shows. For instance, the hydrochloride of the *l*-amine is dextrorotatory in ionising solvents, its rotation being little influenced by the concentration; it is also dextrorotatory in non-ionising solvents at moderately high concentrations, but such solutions on dilution become first optically neutral and then lævorotatory. The implication of these results is briefly discussed, but the available data are at present insufficient for their full interpretation.

IT is known that the stereoisomeric forms of many drugs differ in the intensity of their physiological activity, this difference being shown most markedly by certain optical enantiomorphs, *e.g.*, *d*- and *l*-adrenaline, *d*- and *l*-hyoscyamine. Cushny ("Biological Relations of Optically Isomeric Substances," Baltimore, 1926) has suggested that a clear differentiation in this action of enantiomorphs indicates combination of each with an optically active tissue constituent, the compounds so formed possessing different physicochemical properties and hence different physiological activities. This view has, however, been criticised recently by Ing (*Trans. Faraday Soc.*, 1943, **39**, 372) in the light of the "receptor" theory of drug action.

Monolayer measurements upon suitable optical enantiomorphs should provide a comparatively simple method of testing the validity of Cushny's suggestion. This technique can detect molecular associations of a very labile nature under conditions which approximate to those occurring in biological systems, and mixed monolayers of optically inactive, long-chain, aliphatic acids and similar amines have already been studied in detail by Schulman and his co-workers (cf. *Ann. Reports*, 1939, **36**, 94). We have therefore critically investigated the preparation and optical resolution of two compounds, 1-bromopalmitic acid and 2-amino-*n*-octane, suitable for this purpose; the mixed monolayer properties of the optical enantiomorphs thus obtained are being studied in the Department of Colloid Science, Cambridge University, and the results will be published elsewhere. Meanwhile, we now describe the preparation and resolution of 2-amino-*n*-octane, because its ready isolation makes it a valuable resolving agent in stereochemical work, and because it possesses optical properties of considerable interest.

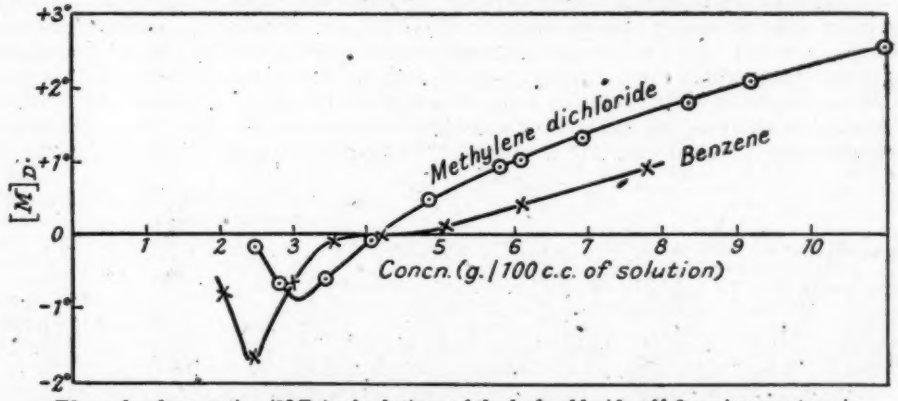
Methyl *n*-hexyl ketone was obtained in *ca.* 95% yield by chromic acid oxidation of 2-hydroxy-*n*-octane (Verhulst and Glorieux, *Bull. Soc. chim. Belg.*, 1932, **41**, 501). The ketone readily furnished the corresponding oxime and *phenylhydrazone*. Reduction of the oxime with sodium and alcohol gave pure 2-amino-*n*-octane in 70% yield and is the best preparative method we have found. Reduction of the phenylhydrazone with sodium amalgam in ethyl alcohol–acetic acid also readily furnished the amine, but even after repeated fractional distillation the amino-octane still contained traces of aniline. The amine is almost insoluble in water, but soluble in most organic solvents.

2-Amino-*n*-octane has been obtained optically active by Levene and Rothen (*J. Biol. Chem.*, 1936, **115**,

415) by the reactions: *d*-2-hydroxy-*n*-octane ⟶ *l*-2-iodo-octane ⟶ *d*-2-azido-octane ⟶ *d*-2-amino-octane. Their amine had $[M]_D^{25°}$ +5·41°, but our results show that it was probably optically impure.*

2-Amino-octane d-*camphorsulphonate*, and d-*bromocamphorsulphonate* underwent no resolution during fractional recrystallisation. The *amine* d-*hydrogen tartrate*, when recrystallised from methyl or ethyl alcohol, however, readily furnished the *l*-amine *d*-hydrogen tartrate, which in turn gave the optically pure l-2-*amino-n-octane*, $[M]_D^{17°}$ −8·53°. Recrystallisation of the *d*-hydrogen tartrate from water gave the d-*amine* d-*hydrogen tartrate*; although after 25 such recrystallisations no further change in rotation of the tartrate could be observed, the regenerated amine had only $[M]_D$ +5·5°, and the optically pure *d*-amine cannot apparently be obtained in this way. The racemic amine was therefore converted into the *l*-hydrogen tartrate, which, recrystallised from methyl alcohol, furnished the *d*-amine *l*-hydrogen tartrate, and the latter then readily gave the optically pure *d*-2-amino-octane, $[M]_D^{17°}$ +8·62°.

The activity of this amine is almost unaffected in benzene solution, but is markedly changed in ethyl-alcoholic solution; *e.g.*, the *d*-amine in 5·95% benzene solution has $[M]_D$ +8·50°, but in 8·06% ethyl-alcoholic solution has $[M]_D$ +0·88°, this value being unaffected by the concentration of the solution (p. 460). This marked change in the optical properties of the amine in alcoholic solution probably indicates a fundamental chemical change (due to association with the solvent) and is discussed later. The change in rotation would probably be shown in other hydroxylic solvents also, and it is particularly unfortunate that the rotation of an aqueous solution cannot be measured owing to the minute solubility of the amine in water.



The molecular rotation ($[M]_D$) *of solutions of the hydrochloride of* l-2-*amino-*n*-octane in methylene dichloride and in benzene.*

The hydrochlorides of the *d*- and the *l*-amine are of particular interest. Not only are they freely soluble in water, and in methyl and ethyl alcohol, but they are also freely soluble in cold methylene dichloride, chloroform, carbon tetrachloride, ethylene dichloride, benzene, toluene, *p*-xylene, and other similar solvents. The solubility in the first group of liquids is, of course, typical of a normal ionised salt, but that in the second group is characteristic of a true covalent compound, and the difference provides a strong indication that the nature of the solvent may profoundly affect the constitution of the hydrochloride.

Furthermore, the hydrochlorides of the active amines show a very pronounced " acid-effect " (cf. Lowry and Baldwin, *Proc. Roy. Soc.*, **1937**, *A*, **162**, 204; Baldwin, *ibid.*, pp. 215, 228; **1938**, *A*, **167**, 539), *i.e.*, the hydrochloride of the *l*-amine is strongly dextrorotatory when dissolved in water, methyl or ethyl alcohol, acetone, formamide, and other solvents. The rotation in ethyl alcohol is almost independent of the concentration of the solution, in marked distinction to that in other solvents discussed below. Baldwin (*loc. cit.*) has shown that most alkyl- and arylalkyl-amines reveal this " acid-effect " on salt formation. It is due to the fact that such free amines have two active absorption bands, one usually at 2400—2000 A., and the second at 1800—1500 A. (cf. Mulliken, *J. Chem. Physics*, **1935**, **3**, 507). The former band owes its existence to the unbound electrons of the nitrogen atom, and the rotatory power of the free amine is due almost entirely to this band alone. On neutralisation of the amine, this band ceases to be circularly dichroic and thus disappears, together (usually) with most of the rotatory power; the rotation of the salt is thus due entirely to the second band, which in many amines may have a rotation of opposite sign to that of the first band. Neutralisation of the amine may therefore cause either a marked decrease in the rotation, or may switch it completely over to the reverse rotation. The *hydrochloride* of our *l*-amine has, *e.g.*, $[M]_D$ +6·61° in 7·77% aqueous solution, $[M]_D$ +7·73° in 6·32% methyl-alcoholic solution, $[M]_D$ +13·9° in 4·310% ethyl-alcoholic solution, and $[M]_D$ +8·65° in 5·02% acetone solution; in all these and many other solvents the " acid-effect " has caused a reversal of sign of rotation, and in ethyl alcohol the *dextro*-molecular rotation has considerably exceeded the *lævo*-molecular rotation of the original undissolved amine.

* In spite of the low rotation of Levene and Rothen's free *d*-amine, the hydrochloride of their amine, in 9·00% aqueous solution, had $[M]_D$ −6·44°, whereas the hydrochloride of our *l*-amine, in 7·77% aqueous solution, had $[M]_D$ +6·61° (p. 460). It is possible, therefore, that Levene and Rothen's products were optically pure, and that their value for the free amine has been incorrectly determined.

The above " acid-effect " can be regarded as a normal property of most aliphatic amines, but the hydrochlorides of our active amines show one strikingly abnormal property. The hydrochloride of *l*-2-amino-octane is dextrorotatory at moderately high concentration in methylene dichloride, ethylene dichloride, chloroform, and benzene, but progressive dilution in each case leads first to optical inactivity and then to a lævorotation, which increases to a limit as dilution proceeds and then necessarily decreases again as the concentration of the salt becomes negligible. The detailed optical data are listed on p. 461, but the curves given illustrate clearly this change of rotation with concentration in benzene and in methylene dichloride solution. This phenomenon must be shown in many other solvents, but the range of solubility is often too small to allow the complete reversal of sign of rotation to be manifest. For instance, solutions in toluene and dioxan that were almost saturated at room temperature were optically inactive, but dilution produced a lævorotation: there is little doubt that had higher temperatures been employed with these solvents to obtain more concentrated solutions, they would have shown a dextrorotation. It is the unusually high solubility of the salt in methylene dichloride and in benzene that allowed the wide range of concentration–rotation measurements (p. 461) to be made. It must be emphasised that there is no question of even slight racemisation affecting the above results: the free amine can be distilled, and its hydrochloride boiled in aqueous solution for 6 hours, without change of activity. Moreover, the hydrochloride used in the above organic solvents was always recovered and its optical purity checked.

These remarkable optical properties of 2-amino-octane and its salts warrant detailed investigation, but until full ultra-violet rotatory dipersion and absorption-spectra measurements can be carried out on the base and its salts in many solvents and at various concentrations, we postpone a full discussion of the results.

It is noteworthy, however, that the hydrochlorides of both the racemic and the *l*-amine are greatly associated in all solvents except those which exert a simple ionising action. This is shown in the following table, where *c* represents the concentration of the solution as g. of solute per 100 g. of solution, and " Eb." and " Cr." represent ebullioscopic and cryoscopic methods of molecular-weight determination; ε is the dielectric constant, and μ the dipole moment of the solvent. The " normal " molecular weight of the hydrochloride is 165·5.

				Hydrochloride of racemic amine.		Hydrochloride of *l*-amine.	
Solvent.	ε.	$\mu \times 10^{18}$.	Method.	*c.*	*M.*	*c.*	*M.*
Water	81·5	1·85	Cr.	2·29	86·9	1·46	87·2
Ethyl alcohol *	25·8	1·70	Eb.	2·40	136	3·312	144
Formamide	—	3·22	Cr.	2·03	81·9	1·83	85·0
Acetonitrile	37·5	3·51	Eb.	3·00	320	2·456	364
Methylene dichloride	9·14	1·55	Eb.	0·539	452	0·646	620
				0·785	511	1·139	628
Chloroform	4·64	1·18	Eb.	0·7079	604	0·6466	606
				1·217	543	0·9745	541
Carbon tetrachloride	2·22	0	Eb.	0·899	559	0·6626	667
				1·318	633	1·716	761
Ethylene dichloride	10·13	1·38	Eb.	1·821	1100	1·550	1820
Ethylene dibromide	4·73	1·12	Cr.	(*a*)	—	0·93	342
Dioxan	2·23	0·45	Eb.	2·325	286	1·936	395
Benzene	2·30	0	Cr.	2·94	808	2·33	792
Toluene	2·38	0·4	Eb.	1·89	680	1·75	709
				2·82	757	3·20	709
p-Xylene	2·27	0	Cr.	1·216	1160	0·835	[2600] (*b*)
				2·128	1180		

* The ethyl alcohol used contained 0·9% of water.
(*a*) The low solubility in freezing ethylene dibromide made measurement impossible.
(*b*) The low solubility in freezing *p*-xylene caused this value to be only approximate.

Whatever the exact interpretation of molecular weights determined by cryoscopic and ebullioscopic methods, there is no doubt about the association of these hydrochlorides in the non-ionising solvents, for our results were obtained with carefully purified solvents, and the molecular depression and elevation constants were based on determinations made with pure solutes (naphthalene, acenaphthene, and diphenyl) at approximately the same molecular concentrations as those used for the amine hydrochlorides in the same apparatus.

The association of many amine salts in various solvents has been critically examined by Turner *et al.* (J., 1911, **99**, 880; 1912, **101**, 1923; 1914, **105**, 1751, 1786; *J. Amer. Chem. Soc.*, 1915, **37**, 2063), who found that, in general, high association occurred in solvents of low dielectic constants, and *vice versa*: our results for the above two hydrochlorides do not, however, follow this rule, and their association must be partly or wholly determined by other factors.

Furthermore, Rule and his co-workers (J., 1931, 674, 2652; 1932, 1400, 1409, 2332; 1933, 376, 1217) have shown that the rotation of a compound in a series of solvents depends largely on the dipole moment of the solvents, since the polar properties of the latter will largely determine the degree of association between the solute and the solvent. It is difficult to detect any similar relationship in our results, where the rotation is so often determined far more by the concentration of the solution than by the polarity of the solvent.

In explanation of our results, we tentatively suggest that the free amine, represented by $R{\cdot}NH_2$, may combine in alcoholic solution with the solvent by hydrogen-bond formation, giving an unstable product

$RH_2N \cdots H{-}OEt$. This would account for the abnormal rotations of alcoholic solutions of the amine, whilst benzene solutions, in which such combination is impossible, show normal rotations. (On the other hand, an addition product of the above structure might be expected to show the " acid-effect," which alcoholic solutions of the amine do not show over the limited range of our measurements : in this respect, however, these solutions may correspond optically to very dilute solutions of the hydrochloride in methylene dichloride, etc.) The amine hydrochloride in aqueous and alcoholic solution undoubtedly has the normal salt structure $[\overset{+}{R}NH_3]\overset{-}{Cl}$. It is possible, however, that in non-ionising solvents such as methylene dichloride and benzene, this salt changes to a similar hydrogen-bond product, $RH_2N \cdots H{-}Cl$, and that it is the resonance between the two hydrogen valencies that makes the compound virtually covalent and hence soluble in such solvents. If this is true, then it is this hydrogen-bond product which associates so readily and must be the essential unit in the molecular aggregates, which may consist of hydrochloride molecules alone, or of the latter associated in addition with solvent molecules.

When a change in concentration of an optically active substance in solution causes a progressive change in the sign of rotation, the substance almost invariably is undergoing some chemical change (*e.g.*, tautomerisation, isomerisation, or combination with the solvent), the degree of change being determined by the concentration. It is highly probable, therefore, that the associated aggregates of the amine hydrochloride in the non-ionising solvents undergo some fundamental change as their solutions are diluted. Since, however, we are ignorant of both the composition and the structure of these micelles, it is useless to attempt to interpret the nature of this change.

Experimental.

All rotations were measured at 17° ± 1°. Those on the free amine (without a solvent) were measured in a 4-cm. tube; all other rotations (*i.e.*, those on all solutions) were measured in a 4-dm. tube.

Methyl n-*Hexyl Ketone*.—Commercial *sec.*-octyl alcohol (120 g., 147 c.c.) was added dropwise during 1·5 hours to a vigorously stirred solution of sodium dichromate dihydrate (90 g.) and concentrated sulphuric acid (120 g., 66 c.c.) in water (600 c.c.). The mixture was then heated under reflux on a boiling water-bath for 2 hours, and the ketone finally isolated by steam distillation : b. p. 172—173°; 110—115 g. (92—96%) (cf. Verhulst and Glorieux, *loc. cit.*).

Methyl n-*Hexyl Ketoxime*.—This was prepared in 90—95% yield and had b. p. 106—108°/12 mm.; Moureu and Delange (*Compt. rend.*, 1903, **136**, 754) give b. p. 116·5°/15 mm.

Reduction. A solution of the oxime (50 g.) in alcohol (200 c.c.) was refluxed on a boiling water-bath during the gradual addition of sodium (75 g., 6 atoms), more alcohol (*ca.* 300 c.c.) being added in small quantities to maintain vigorous reaction. When all the sodium had dissolved, the solution was cooled, diluted with water (250 c.c.), and then gently distilled until the b. p. reached 96°; more water (200 c.c.) was added, and the distillation repeated to ensure complete removal of alcohol, leaving the amine floating on the strongly caustic aqueous solution. (A small quantity of amine was recovered from the distillates and added to this alkaline liquid.) The amine was now extracted from the solution with ether, the solvent removed from the dried extract (sodium hydroxide), and the 2-amino-octane distilled under reduced pressure; b. p. 58—59°/13 mm., 163—164°/760 mm. (Found : C, 74·0; H, 14·6; N, 11·2. Calc. for $C_8H_{19}N$: C, 74·4; H, 14·7; N, 10·9%); 30—32 g. (62—69%).

Reduction of the oxime with sodium amalgam in cold acetic acid, or with aluminium amalgam in warm alcoholic solution (cf. Mann and Pope, *Proc. Roy. Soc.*, 1925, *A*, **107**, 86) gave unsatisfactory results.

The *dl*-amine was characterised by its *benzoyl* derivative, m. p. 73—74° (Found : C, 77·4; H, 10·0; N, 6·0. $C_{15}H_{23}ON$ requires C, 77·4; H, 9·9; N, 6·0%), from aqueous alcohol. Its *hydrochloride*, recrystallised from petrol (b. p. 60—80°), had m. p. 91—92° (Found : Cl, 21·4. $C_8H_{19}N,HCl$ requires Cl, 21·4%).

Methyl n-*Hexyl Ketone Phenylhydrazone*.—Prepared by normal methods, this *phenylhydrazone* was obtained in 65—70% yield as a pale yellow liquid (Found : N, 13·0. $C_{14}H_{22}N_2$ requires N, 12·8%); b. p. 119—120°/0·05 mm. When the crude product was distilled at 12 mm., the hydrazone had b. p. 179—181°, but was impure (Found : N, 11·7%).

Reduction. Best results were obtained by small alternate additions of 2·5% sodium amalgam (600 g.) and glacial acetic acid (100 c.c.) to a solution of the hydrazone (30 g.) in alcohol (300 c.c.) kept below 20°. The product was poured into excess of dilute hydrochloric acid, and alcohol removed by steam-distillation. The residue was basified (sodium hydroxide) and again steam-distilled to isolate the amine, but after the usual procedure, distillation afforded two fractions: (*a*) b. p. 55—64°/13 mm., which after two further fractional distillations afforded 10 g. (60%) of 2-amino-octane, b. p. 58—60°/13 mm., analytically pure (Found : C, 74·0; H, 14·3; N, 11·1%) but still containing a trace of aniline; (*b*) b. p. 65—72°/13 mm., mainly aniline.

dl-2-*Amino*-n-*octane* d-*camphorsulphonate* was obtained by mixing equimolecular quantities of the amine and the acid in alcoholic solution and then evaporating the solvent in a vacuum desiccator, the residual syrupy sulphonate ultimately crystallising. The salt was readily soluble in cold water, methyl and ethyl alcohols, moderately soluble in cold ethyl acetate, but almost insoluble in benzene, toluene, and *cyclo*hexane. After four recrystallisations from ethyl acetate–*cyclo*hexane, the sulphonate was obtained as soapy crystals, m. p. 162—165°, unchanged by further crystallisation (Found : N, 3·9. $C_8H_{19}N,C_{10}H_{16}O_4S$ requires N, 3·9%). A 2·817% aqueous solution had α_D +1·54°, $[M]_D^{18°}$ +49·5°; since a 2% solution of the camphorsulphonate ion has $[M]_D$ +50·0° (Graham, J., 1912, **101**, 746), no resolution was occurring.

The d-α-*bromocamphorsulphonate*, similarly prepared and recrystallised, had m. p. 180—185° (Found : N, 2·9. $C_8H_{19}N,C_{10}H_{15}O_4BrS$ requires N, 3·2%). The amine, liberated from this salt by sodium hydroxide, was optically inactive.

Resolution of the dl-*Amine*.—Full optical data are collected on p. 460. In the following description, only sufficient data are cited to show the course of the resolution.

(A) *Using methyl alcohol*. The *dl*-amine (150 g.) and *d*-tartaric acid (174 g., 1 mol.) were dissolved together in hot methyl alcohol (750 c.c.), and the crystals which separated on cooling were then recrystallised eight times more from methyl alcohol (using 400, 300, 250, 200, 150, 120, 120, 120 c.c. of solvent). The d-*hydrogen tartrate* thus obtained separated as the *hemi-methyl alcoholate* (Found : C, 50·6; H, 9·3; N, 4·85; CH_4O, 5·1. $C_8H_{19}N,C_4H_6O_6,\frac{1}{2}CH_4O$ requires C, 50·8; H, 9·15; N, 4·75; CH_4O, 5·4%); confinement in a vacuum readily gave the solvent-free *salt*, m. p. 75—83° (Found : C, 51·3; H, 8·7; N, 4·85. $C_8H_{19}N,C_4H_6O_6$ requires C, 51·6; H, 9·0; N, 5·0%). A portion of this salt was decomposed with 10% aqueous sodium hydroxide, the liberated amine extracted with ether, and the extract dried over powdered sodium hydroxide. Fractional distillation of the filtered extract, protected from carbon dioxide, in an all-

glass lubricant-free apparatus gave the amine, b. p. 76°/30 mm.; the distillate was finally dried over sodium and then had α_D −2·00°, α_{4358} −3·92°; $[M]_D$ −8·36°, $[M]_{4358}$ −16·4°. This amine was reconverted into the *d*-hydrogen tartrate, added to the main bulk of the salt, and the whole recrystallised again (120 c.c.). A portion now furnished the free amine, α_D −2·04°, α_{4358} −4·02°, $[M]_D$ −8·53°, $[M]_{4358}$ −16·8°. This procedure was repeated, the salt now being recrystallised twice more (100, 100 c.c.); the *d*-hydrogen tartrate had m. p. 75—84° and gave the pure l-*amine*, α_D −2·04°, α_{4358} −4·02°

		Wave length (A.) of light.								
		Li, 6708.	Li, 6104.	Na, 5893.	Hg, 5780.	Hg, 5461.	Hg, 4358.	*k* (calc.).	λ_0^2 (calc.).	λ_0, A.
d-*Amine.*										
(*a*) Without solvent	a, obs.	+1·57°	+1·92°	+2·06°	+2·16°	+2·44°	+4·05°	—	—	—
	[*M*]	6·56	8·03	8·62	9·03	10·2	16·9	—	—	—
	a, calc.	1·57	1·92	2·07	2·16	2·44	4·03	0·6694	0·0238	1540
	a, obs.—a, calc.	0·00	0·00	−0·01	0·00	0·00	+0·02	—	—	—
(*b*) In 5·953% benzene solution	a, obs.	+1·18	+1·47	+1·57	+1·65	+1·84	+3·03	—	—	—
	[*M*]	6·34	7·96	8·50	8·99	9·97	16·4	—	—	—
	a, calc.	1·22	1·47	1·58	1·64	1·84	2·91	0·5441	0·00324	1800
	a, obs.—a, calc.	−0·04	0·00	−0·01	+0·01	0·00	+0·12	—	—	—
(*c*) In 2·77% ethyl alcohol solution	a, obs.	*	*	+0·08	+0·09	+0·11	—	—	—	—
	[*M*]	—	—	0·9	1·0	1·3	—	—	—	—
In 8·06% ethyl alcohol solution	a, obs.	*	*	+0·22	+0·24	+0·32	†	—	—	—
	[*M*]	—	—	0·88	0·96	1·34	—	—	—	—
l-*Amine.*										
(*a*) Without solvent	a, obs.	−1·56	−1·91	−2·04	−2·15	−2·43	−4·02	—	—	—
	[*M*]	6·52	7·98	8·53	8·99	10·2	16·8	—	—	—
	a, calc.	1·56	1·91	2·06	2·15	2·43	4·03	0·660	0·0262	1620
	a, calc.—a, obs.	0·00	0·00	−0·02	0·00	0·00	−0·01	—	—	—
Hydrochloride of d-*amine in* EtOH.										
(i) In 3·08% solution	a, obs.	*	*	−1·00	*	−1·10	*	—	—	—
	[*M*]	—	—	13·4	—	14·8	—	—	—	—
(ii) In 4·29% solution	a, obs.	*	*	−1·44	−1·51	−1·74	−3·13	—	—	—
	[*M*]	—	—	13·8	14·5	16·7	30·0	—	—	—
(iii) In 4·58% solution	a, obs.	*	*	−1·55	*	−1·84	*	—	—	—
	[*M*]	—	—	14·0	—	16·7	—	—	—	—
(iv) In 6·88% solution	a, obs.	*	*	−2·33	*	2·79	*	—	—	—
	[*M*]	—	—	14·0	—	16·8	—	—	—	—
(v) In 10·31% solution	a, obs.	−2·63	−3·28	−3·60	−3·75	−4·26	−7·35	—	—	—
	[*M*]	10·6	13·2	14·5	15·0	17·1	29·5	—	—	—
	a, calc.	2·64	3·28	3·56	3·72	4·27	7·55	1·058	0·0500	2240
	a, obs.—a, calc.	−0·01	0·00	+0·04	+0·03	−0·01	−0·20	—	—	—
(vi) In 15·47% solution	a, obs.	*	*	−5·6	*	−6·9	*	—	—	—
	[*M*]	—	—	14·9	—	18·5	—	—	—	—
Hydrochloride of l-*amine.*										
(*a*) In 7·77% aqueous solution	a, obs.	+0·96	+1·14	+1·24	+1·30	+1·45	+2·42	—	—	—
	[*M*]	5·11	6·08	6·61	6·94	7·74	12·9	—	—	—
	a, calc.	0·93	1·14	1·23	1·31	1·45	2·42	0·3943	0·0266	1630
	a, obs.—a, calc.	+0·03	0·00	+0·01	−0·01	0·00	0·00	—	—	—
(*b*) In 6·32% methyl alcohol solution	a, obs.	+0·88	+1·09	+1·18	+1·24	+1·42	+2·54	—	—	—
	[*M*]	5·76	7·14	7·73	8·12	9·30	16·6	—	—	—
	a, calc.	0·88	1·09	1·18	1·24	1·42	2·58	0·3445	0·0584	2370
	a, obs.—a, calc.	0·00	0·00	0·00	0·00	0·00	−0·04	—	—	—
(*c*) In 4·310% ethyl alcohol solution	a, obs.	+1·08	+1·34	+1·45	+1·51	+1·75	+3·12	—	—	—
	[*M*]	10·4	12·9	13·9	14·5	16·8	29·9	—	—	—
	a, calc.	1·08	1·34	1·45	1·52	1·75	3·16	0·4249	0·0554	2350
	a, obs.—a, calc.	0·00	0·00	0·00	−0·01	0·00	−0·04	—	—	—
(*d*) In 5·02% acetone solution	a, obs.	+0·79	+0·97	+1·05	+1·10	+1·27	+2·29	—	—	—
	[*M*]	6·51	8·00	8·65	9·06	10·5	18·9	—	—	—
	a, calc.	0·78	0·97	1·05	1·10	1·27	2·31	0·3050	0·0580	2410
	a, obs.—a, calc.	+0·01	0·00	0·00	0·00	0·00	−0·02	—	—	—
(*e*) In 5·37% formamide solution	a, obs.	+0·40	+0·50	+0·53	+0·56	+0·65	+1·07	—	—	—
	[*M*]	3·09	3·96	4·09	4·32	5·01	8·26	—	—	—
	a, calc.	0·40	0·50	0·54	0·57	0·65	1·09	0·1577	0·0572	2390
	a, obs.—a, calc.	0·00	0·00	−0·01	−0·01	0·00	−0·02	—	—	—
(*f*) In 3·180% acetonitrile solution	a, obs.	*	*	+0·69	+0·73	+0·81	+1·43	—	—	—
	[*M*]	—	—	8·95	9·48	10·5	18·6	—	—	—
(*g*) In 2·31% carbon tetrachloride solution	a, obs.	*	*	+0·55	*	*	*	—	—	—
	[*M*]	—	—	9·85	—	—	—	—	—	—
In 4·17% carbon tetrachloride solution	a, obs.	*	*	+1·17	+1·24	+1·44	+2·44	—	—	—
	[*M*]	—	—	11·6	12·3	14·3	24·2	—	—	—
(*h*) In 2·16% chloroform solution	a, obs.	*	*	−0·08	*	*	*	—	—	—
	[*M*]	—	—	1·5	—	—	—	—	—	—
In 4·45% chloroform solution	a, obs.	*	*	+0·09	+0·10	+0·13	+0·22	—	—	—
	[*M*]	—	—	0·8	0·94	1·2	2·05	—	—	—

* Not measured. † Not observable.

(Found: N, 10·6%). The resolution had thus been complete after the tenth recrystallisation. The tartrate in the mother-liquors of the last two recrystallisations was therefore recovered, added to the final fraction, and the pure *l*-amine liberated; 12·5 g. It is noteworthy that the m. p. of the tartrate is not markedly affected by the optical purity of the salt and so gives no reliable indication of the course of the resolution.

The mother-liquors from the first four above recrystallisations were evaporated, and the amine liberated from the residue had α_D +0·52°. This was converted into the *l*-hydrogen tartrate, and the latter recrystallised seven times from methyl alcohol. The product, treated as before, furnished the optically pure *d*-amine, b. p. 70°/25 mm., α_D +2·06°, α_{4358} +4·05°; $[M]_D$ +8·62°, $[M]_{4358}$ +16·9°; 6·0 g. Further recrystallisation of the tartrate did not change the rotation of the liberated amine.

(B) *Using ethyl alcohol.* When the *d*-hydrogen tartrate of the *dl*-amine was prepared as above, but in ethyl alcohol, the *l*-amine *d*-hydrogen tartrate was again the less soluble; 13 or 14 recrystallisations (depending on the volume of solvent used) were, however, now required to complete the resolution and to furnish the optically pure *l*-amine. The use of methyl alcohol is therefore preferable.

(C) *Using water.* Earlier work showed that recrystallisation of the *d*-hydrogen tartrate of the *dl*-amine from water furnished the less soluble d-*amine* d-*hydrogen tartrate*. This resolution was therefore investigated in detail, as it appeared a valuable alternative to the use of the costly *l*-tartaric acid. The *dl*-amine (463 g.) and *d*-tartaric acid (549 g., 1 mol.) were dissolved together in boiling water, and the crop of hydrogen tartrate which separated was recrystallised thrice more from water; m. p. 78—82° (Found: C, 51·2; H, 8·8; N, 5·0%). The amine, liberated from a portion of this salt, had α_D +0·08°. The salt was then repeatedly recrystallised from water. Test samples showed a steadily increasing rotation of the liberated amine until the salt had been recrystallised 23 times; the liberated amine now had b. p. 55—56°/12 mm., α_D +1·32°, $[M]_D$ +5·5°. Further recrystallisations of the salt did not sensibly affect the rotation of the liberated amine, and this method of resolution was therefore abandoned.

The *hydrochloride* of the *l*-amine was prepared by neutralising the amine with dilute hydrochloric acid and evaporating the solution in a vacuum at room temperature; the residual solid, recrystallised from petrol (b. p. 60—80°), had m. p. 90—91° (Found: Cl, 21·6. $C_8H_{19}N,HCl$ requires Cl, 21·4%). The hydrochloride of the *d*-amine, similarly prepared, also had m. p. 90—91°.

The *benzoyl* derivative of the *l*-amine recrystallised from *cyclo*hexane as colourless needles, m. p. 101—102° with slight preliminary softening (Found: N, 6·1. $C_{15}H_{23}ON$ requires N, 6·0%). It is appreciably less soluble in *cyclo*hexane than the racemic compound.

In the optical rotation data given below, the rotation constant (k) and the dispersion constant (λ_0) have been calculated throughout on the simple dispersion equation $\alpha = k/(\lambda^2 - \lambda_0^2)$. It must be emphasised, however, that our measurements of the rotatory dispersion, being limited to six wave-lengths in the visible spectrum, provide too narrow a basis for accurate calculation of the dispersion constants, and the values recorded are necessarily only approximate. For this reason, the dispersion constants have not been calculated when less than the full six readings were made.

In the following solvents, the concentration (c, g. of solute/100 c.c. of solution) of the hydrochloride of the *l*-amine has been varied, but the rotations have been measured solely for the Na_D light. Rotations measured at very great dilution, or at concentrations near the change of sign, were necessarily very small, and high accuracy cannot be claimed for these readings; they indicate clearly, however, the nature of the change of rotation. Great care was necessary to ensure that the solutions were anhydrous.

Methylene dichloride.

c	2·44	2·80	3·36	4·04	4·85	5·82	6·11	6·98	8·38	9·17	11·0
α, obs.	−0·01°	−0·05°	−0·05°	−0·01°	+0·06°	+0·13°	+0·15°	+0·21°	+0·35°	+0·46°	+0·66°
$[M]$	−0·2	−0·7	−0·6	−0·1	+0·5	+0·92	+1·0	+1·24	+1·73	+2·1	+2·5

Benzene.

c	2·04	2·45	2·94	3·53	4·24	5·09	6·11	7·73
α, obs.	−0·04°	−0·10°	−0·05°	−0·01°	0°	+0·01°	+0·06°	+0·17°
$[M]$	−0·8	−1·7	−0·7	−0·1	0	+0·1	+0·4	+0·91

	Ethylene dichloride.			*Toluene.*		*Dioxan.*		*Ethylene dibromide.*
c	2·23	3·35	5·03	2·28	3·20	2·02	2·66	2·75
α, obs.	−0·02°	+0·08°	+0·30°	−0·08°	0°	−0·05°	0°	0°
$[M]$	−0·4	+1	+2·5	−1·5	0	−1	0	0

Optical Stability.—A 5·31% aqueous solution of this hydrochloride, having α, obs. +0·65°, $[M]$ +5·1°, was refluxed for 6 hours; the solution when cold, still had α, obs. +0·65°, $[M]$ +5·1°.

Benzoyl derivative of l-amine.	λ, A.	6708.	6104.	5893.	5780.	5461.	4358.	k (calc.).	λ_0^2 (calc.).	λ_0, A.
In 1·950% ethyl alcohol solution	α, obs.	−1·62°	−1·92°	−2·08°	−2·17°	−2·46°	−4·20°	—	—	—
	$[M]$	48·4	57·3	62·1	64·8	73·5	125	—	—	—
	α, calc.	1·56	1·92	2·08	2·16	2·46	4·17	0·6501	0·0339	1840
	α, obs.−α, calc.	−0·06	0·00	0·00	+0·01	0·00	+0·03	—	—	—

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124. (I) *The Mechanism of the Cleavage of Ethers of the Anisole Type by Grignard Mixtures.* (II) *The Action of Grignard Solutions on α-Bromo-ketones.*

By Alexander Schönberg and Radwan Moubasher.

(I) Anisole and related substances undergo scission when heated with Grignard mixtures (*i.e.*, mixtures obtained when ethereal Grignard solutions are evaporated to dryness at about 200°). This cleavage was generally attributed to the action of the organic magnesium compound on the substance concerned (compare scheme A), but it is now suggested that the cleavage is effected by the magnesium halide present in the equilibrium $2RMgI \rightleftarrows MgR_2 + MgI_2$, for the same result is obtained with magnesium iodide or bromide alone under the same conditions (compare scheme B).

(II) α-Bromo-ketones when heated with ethereal Grignard solutions (followed by hydrolysis) yield the corresponding unbrominated ketones [cf. *inter alia* (II) ⟶ (IV)]. We attribute these changes, not to the action of Grignard compounds, as formerly believed, but to that of the magnesium halide present in the Grignard solutions.

(I) *Mode of Action of Grignard Mixtures on Anisole and Related Substances.*—The action of Grignard mixtures (see above) on anisole and related substances has been attributed by many workers to the effect of the organo-magnesium halide, which is supposed to form a derivative of a phenol as in (A), proposed by Grignard and Ritz (*Bull. Soc. chim.*, 1936, **3**, 1181). Here (R, R′) represents various aliphatic by-products.

(A) $Ar{-}O{-}CH_3 \longrightarrow Ar{-}O{-}Mg{-}X + (R,R')$

$X{-}Mg \quad R'$

Although this view cannot be disproved, there is no experimental evidence for it, and since we find that magnesium iodide effects cleavage of anisole under the same conditions, and this iodide is known to exist in equilibrium with the Grignard compounds (see above), it seems reasonable to regard this as the active agent, thus:

(B) $PhOMe + MgI_2 \longrightarrow [MgI{\cdot}OPhMe]^+ [I]^- \xrightarrow[\text{decompn.}]{\text{auto-}} Ph{\cdot}O{\cdot}MgI + MeI$

Application of the New Theory to Special Cases.—(*a*) Grignard and Ritz (*loc. cit.*) found that alkylmagnesium iodides react much more rapidly with anisole than do the bromides. On our theory, therefore, magnesium iodide should be more effective than the bromide, and this deduction was verified.

(*b*) *Action of Grignard solutions on phenyl allyl ether.* Lüttringhaus, von Sääf, and Hauschild (*Ber.*, 1938, **71**, 1673) noted that this ether reacts with *n*-butylmagnesium bromide at 50—70°, whereas scission of anisole requires a temperature of 160—200°, and they proposed the scheme (R = *n*-butyl):

(C) $MgRX + PhO{\cdot}CH_2{\cdot}CH{:}CH_2 \longrightarrow PhO{\cdot}MgX + CH_2R{\cdot}CH{:}CH_2$

If our theory be true, phenyl allyl ether should be split by magnesium iodide or bromide alone at similarly low temperatures. This deduction, too, has been verified, and we suggest that a scheme analogous to (B) is valid. It is true that the yield with magnesium bromide alone is smaller than with *n*-butylmagnesium bromide, but we attribute this to the effect of the allyl bromide. Under our conditions, this does not escape (at 50—70°) and so tends to reverse the reaction, whereas under the normal Grignard conditions it reacts with the *n*-butylmagnesium bromide (see D) and so cannot suppress the main reaction.

(D) $MgRBr + CH_2Br{\cdot}CH{:}CH_2 \longrightarrow MgBr_2 + CH_2R{\cdot}CH{:}CH_2$ (I.) (R = *n*-butyl)

Confirmation of this view may be found in the fact that Lüttringhaus *et al.* (*ibid.*, p. 1679) stated that *n*-heptene (I) is formed in 37% yield by the action of ethereal butylmagnesium bromide solutions on phenyl allyl ether at 58°.

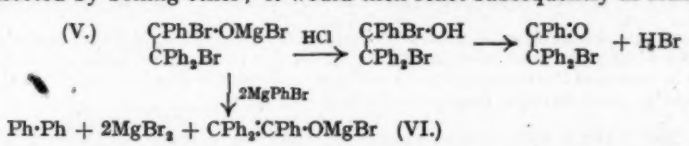
(II) *The Mode of Action of Grignard Solutions on α-Bromo-ketones.*—It is well known that α-bromo-ketones are converted into the corresponding unbrominated ketones by the action of Grignard reagents followed by hydrolysis. This reaction has been expressed in various forms (see, *e.g.*, Kohler and Johnstin, *Amer. Chem. J.*, 1905, **33**, 45; Umnowa, *Chem. Zentr.*, 1913, **84**, I, 1402; Löwenbein and Schuster, *Annalen*, 1930, **481**, 106; Kohler and Tishler, *J. Amer. Chem. Soc.*, 1932, **54**, 1594), and Löwenbein and Schuster believe that free radicals play a part in it, but all the authors agree in attributing the result to the organo-magnesium compound present in the Grignard reagent.

We believe that there is no experimental evidence for this opinion, and that, as before, the reaction is due to the magnesium halide. Our experiments were carried out with benzoyldiphenylbromomethane (II), which is easily accessible and has been widely used in previous researches on this type of reaction.

(*a*) *Action of ethereal magnesium iodide on benzoyldiphenylbromomethane* (II). The first product of this reaction is (III); then free halogen is split off to give (III*a*) (autodecomposition), and treatment of the latter with dilute hydrochloric acid yields benzoyldiphenylmethane (IV) quantitatively. The following scheme is proposed:

(E) $\underset{\text{(II.)}}{CPh{:}O\ CPh_2Br} \xrightarrow{MgI_2} \underset{\text{(III.)}}{CPhI{\cdot}OMgI\ CPh_2Br} \xrightarrow[\text{ether}]{\text{in boiling}} IBr + \underset{\text{(III}a\text{.)}}{CPh{\cdot}OMgI\ CPh_2} \xrightarrow{HCl} \underset{\text{(IV.)}}{CPh{:}O\ CPh_2H}$

(*b*) *Action of ethereal magnesium bromide on benzoyldiphenylbromomethane* (II). Use of magnesium bromide instead of iodide in the above experiment (with ether as a solvent) afforded unchanged starting material. Nevertheless, we believe the primary reaction to be essentially the same as in (E), but the analogue (V) of (III) to be unaffected by boiling ether; it would then react subsequently as follows:



In the presence of Grignard compounds, however, (V) reacts to give (VI), which on acidification affords (IV) (compare the action of phenylmagnesium bromide on dibromostilbene, Kohler and Johnstin, *Chem. Zentr.*, 1905, I, 523: $CHBrPh{\cdot}CHBrPh + 2MgPhBr \longrightarrow CHPh{:}CHPh + Ph{\cdot}Ph + 2MgBr_2$).

(*c*) *Action of magnesium bromide* (*dissolved in warm anisole*) *on benzoyldiphenylbromomethane* (II). If magnesium bromide is allowed to act on (II) (both reagents being dissolved in anisole) at 85°, a product is formed which yields benzoyldiphenylmethane when treated with hydrochloric acid, the reaction being analogous to that in (E). The addition product (V), which is formed in ethereal as well as in anisole solution, is stable at the b. p. of ether, but decomposes at higher temperatures.

Experimental.

(I) *Action of Magnesium Iodide on Anisole.*—This experiment, analogous to that of Simonis and Remmert (*Ber.*, 1914, **47**, 269) using a dried Grignard reagent, was carried out in a vessel fitted with a reflux condenser to which a calcium chloride tube was connected. Magnesium powder (9·7 g.), suspended in 250 c.c. of ether (distilled over sodium), was treated portionwise with iodine (50·8 g.) in the cold; reaction took place immediately, and the mixture was refluxed until almost colourless, excess of magnesium then being filtered off. The ether was evaporated, and during this process anisole (10·8 g.) was added gradually, and the mixture heated, in a vessel fitted with an air condenser, in an oil-bath at 200—220° for one hour. No anisole could then be detected, and the residue was red; after having cooled, it was decomposed with dilute hydrochloric acid, rendered alkaline, and extracted with ether. The aqueous alkaline layer was separated, warmed to expel traces of ether, acidified, and steam-distilled. The distillate was made alkaline and treated with excess of benzoyl chloride in the cold. A crystalline precipitate was formed, and after 15 minutes the reaction mixture was poured into iced water. Phenyl benzoate (11·5 g.) was obtained and crystallised from benzene; m. p. 68°, undepressed on admixture with an authentic specimen. Simonis and Remmert had obtained phenoxymagnesium iodide (see scheme A).

Action of Magnesium Bromide on Anisole.—The magnesium bromide was prepared from bromine (12 g.) and excess of magnesium powder, the conditions and subsequent procedure being as for the iodide (above), except that 20 g. of anisole were used. Phenyl benzoate was obtained in much smaller yield.

Action of Magnesium Bromide on Phenyl Allyl Ether at 95°.—The phenyl allyl ether (Perkin, J., 1896, **69**, 1225) was carefully purified and freed from any traces of phenol. To an ethereal solution of magnesium bromide, prepared as described above (bromine, 32 g.; magnesium, 9·8 g.; ether, 250 c.c.), anisole (30 g.) was added, and the mixture heated to remove the ether. Phenyl allyl ether (13·5 g.) was added, and the mixture heated for 5 hours at 95°, a stream of dry carbon dioxide being passed through it in order to remove the allyl bromide formed. (All these processes were carried out in a dry atmosphere.) The mixture was allowed to cool, and shaken with ammonium chloride solution; aqueous sodium hydroxide solution was then added in excess, and the mixture again shaken and left for several hours. The aqueous layer was separated, acidified, and steam-distilled, and the distillate rendered alkaline and treated with benzoyl chloride. Phenyl benzoate (3·5 g.) was obtained (identified by mixed m. p.).

In two blank experiments, one without magnesium bromide and the other without phenyl allyl ether, phenyl benzoate was not formed.

(II) *Action of Magnesium Iodide on Benzoyldiphenylbromomethane* (II) *in Boiling Ether* (with Miss Soad Bedeir).—To a filtered ethereal solution of magnesium iodide, prepared as above from iodine (4 g.) and ether (150 c.c.), benzoyldiphenylbromomethane (0·5 g.) was added, and the solution refluxed for 6 hours. The mixture was then treated with dilute hydrochloric acid and ice, the ethereal layer separated, and dried over sodium sulphate; the ether was distilled off, and the residue crystallised from petrol (b. p. 60—70°), colourless crystals of benzoyldiphenylmethane being obtained, m. p. and mixed m. p. 137°, in almost quantitative yield. In a blank experiment carried out without magnesium iodide, the initial substance was recovered unchanged.

Magnesium Bromide and Benzoyldiphenylbromomethane (II) *in Boiling Ether.*—A solution of magnesium bromide (bromine, 4 g.; magnesium, 1·2 g.; ether, 150 c.c.) was prepared (in diffused light), the bromo-compound added, and the solution refluxed for 9 hours in a dry atmosphere. After treatment with dilute hydrochloric acid and ice, followed by ether extraction as usual and distillation, (II) was recovered unchanged; m. p. and mixed m. p. 97°.

Action of Magnesium Bromide on Benzoyldiphenylbromomethane in the Presence of Warm Anisole.—An ethereal solution of magnesium bromide was prepared as above, and the ether distilled off; during this distillation anisole (10 g.) was added in portions. When all the ether had been driven off, benzoyldiphenylbromomethane (0·5 g.) was added, and the reaction mixture heated under reflux (guard tube) on a water-bath for 9 hours. (The temperature of the mixture did not exceed 85°.) The product was worked up in the usual manner, the ether and most of the anisole being removed in a vacuum on a water-bath. The residue solidified (m. p. 135°), and after recrystallisation from petrol (b. p. 100—150°), had m. p. and mixed m. p. with benzoyldiphenylmethane 136°.

The bromo-compound (II) was heated on the water-bath with anisole for 3 hours, the anisole driven off in a vacuum, and the residue cooled; the initial substance was found to be unchanged.

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125. *Formation and Structure of Some Organic Molecular Compounds. Part III. The Dielectric Polarisation of Some Solid Crystalline Molecular Compounds.*

By H. Kronberger and J. Weiss.

The mean dielectric constants of a number of polynitro-molecular compounds, of quinhydrone, and of their respective components in the solid state have been measured in the Hertzian region by an immersion method. This furnishes new evidence in favour of the ionic character of these molecular compounds which is also supported by the discussion of some of the other physical properties in the solid state.

In Parts I and II (J., 1942, 245; 1943, 462) it was suggested that the bonding in molecular compounds of molecules with systems of conjugated double bonds (*e.g.*, polynitro-compounds, quinones, etc.) is ionic or at least partly ionic in character. This was supported by the experimental evidence then available (*e.g.*, dipole moments, electrical conductivity) for certain molecular compounds in solution, but the fact that all such compounds in solution are to some extent dissociated into their components, together with their comparatively low solubilities, made it desirable to investigate some properties of the solid molecular compounds.

The *X*-ray work by Hertel *et al.* is compatible with the ionic structure, as was shown in Part I (*loc. cit.*), although it is, of course, practically impossible to deduce anything definite about the character of the bond in these complicated molecules from a determination of the crystal structures alone. Powell and Huse's work (J., 1943, 153, 435) is not conclusive, particularly as they investigated only two compounds (which are not representative) and in both cases the donor molecule had an electronegative iodine atom as a substituent. Powell (Report on the Conference of the *X*-Ray Analysis Group of the Institute of Physics, *Nature*, 1944, 153, 533) also has now concluded that some of the interatomic distances recorded are too small to be accounted for by van der Waals forces.

The m. p.'s of molecular compounds with large, polarisable molecules cannot be expected to behave in the same way as those of simple ionic crystals, although the m. p.'s of the molecular compounds are often higher than those of their components. Even simple metal halides with layer lattices often show comparatively low m. p.'s. According to Hund (*Z. Physik*, 1925, **34**, 833), this is due to the fact that in these cases the process of melting only means a destruction of the lattice into polar molecules without a separation into the ions. A similar state of affairs presumably exists in the case of some molecular compounds.

In the absence of any quantitative measurements on the hardness of molecular compounds, nothing can be said about this at present although it is clear, particularly from the extensive work of Reis and Zimmermann (*Z. physikal. Chem.*, 1922, **102**, 298), that in organic substances no simple relation exists between hardness and ionic structure. On the other hand, Kochendörfer (*Z. Krist.*, 1934, *A*, **97**, 263, 280; *Z. Physik*, 1937, **108**, 264) has recently found that the mechanical behaviour (*e.g.*, slip-hardening) of some organic crystals (*e.g.*, naphthalene) is quite similar to that of simple ionic crystals or metals.

The characteristic properties of ionic crystals are revealed by certain optical measurements (*e.g.*, absorption in the infra-red) and by their dielectric properties (cf. Born and Göppert-Mayer, "Handbuch der Physik," 2nd edn., XXIV/2), but very little information is yet available about the dielectric constants of organic crystals.

We now report some of the dielectric properties of a number of molecular compounds and of their components. We have actually measured the (mean) dielectric constants of these substances in the form of crystalline powders. The measurements were carried out by an immersion method which was originally proposed by Starke (*Ann. Physik*, 1897, **60**, 629, 641) and later used by Eucken and Büchner (*Z. physikal. Chem.*, 1934, *B*, **27**, 321) and by Højendahl (*K. Danske Vidensk Selskab.*, 1938, **16**, No. 2) for the determination of dielectric constants of inorganic salts. However, the metal–glass cells described by these authors were found very unsatisfactory for our purpose and we have developed two new types of all-glass cells with burnt-on platinum electrodes. One of the cells could be used for very small amounts of substance (0·05—0·1 g.). Special care was taken to ensure a random distribution of the small crystals between the electrodes of the condenser cells. The (mean) dielectric constants determined in this way with different samples in different immersion liquids and in the two different cells were reproducible within $\pm 0{\cdot}5\%$. The measurements were carried out at a temperature of $17° \pm 1{\cdot}0°$ and at radio frequencies (about 800 kc./sec.), a double heterodyne method being used.

In Table I the (mean) dielectric constants (ε) of the substances investigated are given. The densities of the solids (d) were taken from the literature or determined by a flotation method (see Experimental). The molecular polarisations of the molecular compounds, $P^{(AB)}$, and of the components, $P^{(A)}$ and $P^{(B)}$, were calculated according to the formulæ of Lorentz–Lorenz and of Drude, (1) and (2), respectively:

$$P_{(L)} = \frac{\varepsilon - 1}{\varepsilon + 2} \cdot \frac{M}{d} = \frac{4}{3}\pi N\gamma_{(L)} \quad \ldots \quad (1)$$

$$P_{(D)} = \frac{\varepsilon - 1}{3} \cdot \frac{M}{d} = \frac{4}{3}\pi N\gamma_{(D)} \quad \ldots \quad (2)$$

M being the molecular weight, N Avogadro's number, and γ the total polarisability per molecule.

The formula (1) was derived for isotropic media or for complete random distribution, but modern theory generally favours (2), which, according to Mott and Gurney ("Electronic Processes in Ionic Crystals," Oxford Univ. Press, 1940), even in simple ionic crystals gives a much better account of the facts if the electronic

TABLE I.

Dielectric Constants and Corresponding Molecular Polarisations.

Substance.	*M.*	*d.**	ε.	$P_{(L)}$.	$P_{(D)}$.
Anthracene	178	1·245 [1]	3·46	64·1	116·7
Benzidine	184	1·39	3·61	61·6	115·3
3 : 4-Benzpyrene	252	1·351	3·52	85·1	156·7
Chrysene	228	1·27 [2]	3·32	78·1	138·6
Coronene	300	1·37	3·38	96·9	173·7
Quinol	110	1·33 [3]	3·58	38·0	71·2
20-Methylcholanthrene	268	1·277 [4]	3·53	96·1	177·0
Naphthalene	128	1·158 [1]	3·07	45·2	76·2
Phenanthrene	178	1·175	3·01	60·7	101·3
p-Phenylenediamine	108	1·205	3·95	44·4	88·0
Picric acid	229	1·764 [5]	3·59	60·1	112
Pyrene	202	1·27	3·21	67·5	117·3
Benzoquinone	108	1·31 [3]	3·12	34·1	58·1
s-Trinitrobenzene	213	1·687	3·00	50·4	84·0

Molecular compound.	*M.*	*d.*	ε.	$P_{(L)}$.	$P_{(D)}$.
(A) Anthracene–picric acid	407	~1·50	3·29	117	207
(B) Anthracene–*s*-trinitrobenzene	391	1·40	3·25	119·6	209·7
(C) Benzidine–*s*-trinitrobenzene	397	1·45	3·47	121·2	225·3
(D) 3 : 4-Benzpyrene–*s*-trinitrobenzene	465	1·475	3·20	133·3	231·3
(E) Chrysene–*s*-trinitrobenzene	441	1·420	3·12	128·6	219·7
(F) *Coronene–s-trinitrobenzene*	513	1·455	3·40	156·7	282·0
(G) 20-Methylcholanthrene–*s*-trinitrobenzene	481	1·446	3·32	145·0	257·0
(H) Phenanthrene–*s*-trinitrobenzene	391	1·432	3·04	111·0	186·3
(I) *p*-Phenylenediamine–*s*-trinitrobenzene	321	1·425	3·91	110·7	218·3
(J) *Pyrene–s-trinitrobenzene*	415	1·50	3·20	117·0	202·7
(K) Quinhydrone	218	1·401 [6]	4·12	79·3	162·0

* The densities were determined by the authors unless otherwise stated.

[1] Neuhaus, *Ber.*, 1934, **67**, 1627. [2] Iball, *Proc. Roy. Soc.*, 1934, *A*, **146**, 140. [3] Caspari, *ibid.*, 1932, *A*, **136**, 82. [4] Iball, *Z. Krist.*, 1936, **94**, 7. [5] Rudolfi, *Z. physikal. Chem.*, 1909, **66**, 705. [6] Siegmund, *Monatsh.*, 1909, **29**, 1091.

structures overlap each other, and this certainly holds for the ions present in the molecular compounds. Recently the matter has been discussed by Darwin (*Proc. Roy. Soc.*, 1943, *A*, **182**, 152), who concludes that Drude's formula gives a far better approximation also for an assembly of ionised molecules.

Table II shows that there are sometimes considerable differences between the molecular compounds and the sum of the polarisations of their respective components.

TABLE II.

Deviations from Additivity.

Comparison of the polarisations of the molecular compounds, $P^{(AB)}$, with the sum of the polarisations, $P^{(A)} + P^{(B)}$, of the components.

Molecular compound (see Table I).	$\{P^{(A)} + P^{(B)}\}_L$.	$P_{(L)}^{(AB)}$.	$\Delta P_{(L)}$.	Deviation, %	$\{P^{(A)} + P^{(B)}\}_D$.	$P_{(D)}^{(AB)}$.	$\Delta P_{(D)}$.	Deviation, %
(A)	124·2	117·0	−7·4	−5·9	229·0	207·0	−22·0	−10·0
(B)	114·5	119·6	5·1	4·5	200·7	209·7	9·0	4·5
(C)	112·0	121·2	9·2	8·2	199·3	225·3	26	13
(D)	135·5	133·3	−2·2	−1·6	240·7	231·3	− 9	− 5
(E)	128·5	128·6	0·1	0·1*	222·6	219·7	− 2·9	− 1·3
(F)	147·3	156·7	9·4	6·8	257·7	282·0	24·3	9·9
(G)	146·5	145·0	−1·5	−1·0	261	257	− 4·0	− 2·0
(H)	111·1	111·0	−0·1	−0·1	185·3	186·3	1·0	0·5
(I)	94·8	110·7	15·9	16·8	172·0	218·3	46·3	27·0
(J)	117·9	117·0	−0·9	−0·8	201·0	202·7	1·7	1·0
(K)	72·3	79·3	7·0	9·7	129·3	162·0	32·7	25·3

DISCUSSION.

In the case of van der Waals forces one should get at least an approximate additivity of the molecular polarisations. If, on the other hand, the formation of the molecular compound is accompanied by electronic changes, *e.g.*, by an electron transfer of the type

$$\underset{\text{(donor)}}{A} + \underset{\text{(acceptor)}}{B} \rightleftarrows (A^+B^-) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

deviations from additivity must be expected. Table II shows that the deviations can be positive or negative in character. The approximate additivity observed in a few cases may then be regarded as more or less accidental (the positive and negative effects cancelling each other). These effects can be easily interpreted from a theoretical point of view. The measurements were carried out at radio-frequencies and sufficiently far from the m. p.'s for orientation (or rotation) effects to be neglected. In this case a lattice of ions is distorted in two

different ways in an electric field: (i) Distortion of the electronic clouds of the ions by the external field, which is practically independent of the lattice—this gives rise to the electronic polarisation (P_E). (ii) Displacement of the positive and negative ions (in opposite directions) in the quasi-static external field and also a change of the total electric moment in the field of the ions of the lattice. Actually, every possible interionic or intramolecular vibration between the ions, atoms, and radicals gives rise to a corresponding term in the polarisation of the heavy particles, $P_{(IAR)}$. Thus:

$$P_{(IAR)} = P_I + P_A + P_R \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

(cf. Errera, "Polarisation diélectrique," Paris, 1928; Fuchs and Wolf, "Dielektrische Polarisation," Leipzig, 1935).

The dielectric constant measured at radio-frequencies gives the total polarisation (P) according to

$$P = P_E + P_{(IAR)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The electronic polarisation (P_E) can be measured optically by means of the refractive index (in the near infrared), since the displacement of the electrons follows the rapidly varying field of the electromagnetic light waves. In the absence of vibrating ions, atoms, or radicals the last term in equation (5) disappears, and the dielectric constant in the Hertzian region should become identical with the one deduced from the refractive index (n) according to Maxwell's equation ($\varepsilon_0 = n^2$).

Intermolecular changes accompanying the formation of the molecular compounds are without appreciable influence on the electronic polarisation. However, any changes in the structure of the electronic clouds of the constituents must be of considerable importance. Whereas the two components enter as uncharged molecules, they are transformed into ions in the molecular compound. The fields of the positive and negative charges now present have a profound effect on the electronic clouds of these highly polarisable molecules. It is clear that the introduction of a positive charge will result in a "hardening" of the electron cloud which expresses itself in a decrease of the electronic polarisation and (electronic) polarisability (α), whereas a negative charge will cause a "softening" of the electron cloud of the molecule in which it is present.

The general effect of electric fields on the polarisability has been discussed by Hellmann ("Einführung in die Quantenchemie," Vienna, 1937, p. 172), who has also given an approximate expression (valid only for homogeneous fields). He has shown that the effective polarisability ($\alpha_{eff.}$) in the presence of a strong field depends on the polarisability (α) in the "unstrained" state and on the field strength. It is clear that $\alpha_{eff.} < \alpha$ for positive charges, whereas $\alpha_{eff.} > \alpha$ for negative charges. This effect has also been discussed by Born and Heisenberg (*Z. Physik*, 1924, **23**, 388) and by Smyth ("Dielectric Constant and Molecular Structure," The Chemical Catalog Co. Inc., 1931).

A second-order effect of a similar type is also known from the work of Fajans, Joos, and others (cf. Hellmann, *loc. cit.*), who found that the refraction of ions, *e.g.*, in ionic crystals, is not constant but changes on the formation of the crystal or of a polar molecule. It has been shown particularly by Neugebauer (*Z. Physik*, 1935, **94**, 655) that this is due to the influence of the field of the positive ion on the electronic cloud of the negative ion and *vice versa*. However, this effect is small compared with that in the case of the molecular-compound formation, where there is no field at all present at first and the change is from neutral to charged. In the case of the molecular compounds this will be only a second-order term somewhat decreasing the primary effect (as the positive charge of the cation is partly neutralised by the electron cloud of the anion and *vice versa*).

For the difference in the electronic polarisability (ΔP_E) on account of molecular-compound formation according to equation (3) one finds

$$\Delta P_E = P_E^{(AB)} - (P_E^{(A)} + P_E^{(B)}) = (P_E^{(A^+)} + P_E^{(B^-)}) - (P_E^{(A)} + P_E^{(B)}) \quad . \quad . \quad . \quad . \quad (6)$$

or

$$\Delta P_E = -\Delta P_E^{(A)} + \Delta P_E^{(B)} = -(P_E^{(A)} - P_E^{(A^+)}) + (P_E^{(B^-)} - P_E^{(B)}) \quad . \quad . \quad . \quad (6a)$$

where $P_E^{(A+)}$ and $P_E^{(B-)}$ denote the effective polarisations under the influence of the electric fields concerned. It is clear that $P_E^{(A+)} < P_E^{(A)}$ ("hardening") and $P_E^{(B-)} > P_E^{(B)}$ ("softening").

In the term $P_{(IAR)}$ (due to the heavier particles) it is useful to distinguish between intra- and inter-molecular (or interionic) changes of the polarisations due to the formation of the molecular compound. It is clear that here the main contribution will be due to the ionic polarisation, $P_I^{(AB)}$, of the ions formed, and that any intermolecular changes will be small compared with this term. We may, therefore, write as a first approximation for the difference of the vibrational polarisation terms, $\Delta P_{(IAR)}$, in molecular-compound formation

$$\Delta P_{(IAR)} = P_{(IAR)}^{(AB)} - [P_{(IAR)}^{(A)} + P_{(IAR)}^{(B)}] \approx P_I^{(AB)} \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

if we neglect the small differences in the intramolecular terms.

From equations (6) and (7) one obtains for the change of the total molecular polarisation on molecular-compound formation:

$$\Delta P = \Delta P_E + \Delta P_{(IAR)} \cong -\Delta P_E^{(A)} + \Delta P_E^{(B)} + P_I^{(AB)} \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

The value of ΔP can be positive or negative, which is borne out by the experiments (Table II). Larger negative deviations are to be expected if the original donor molecule is comparatively small and more polarisable than the acceptor molecule.

The situation is essentially the same if only a partial electron transfer takes place, because it is not the true

charge (e) which matters but the change of the electric moment (μ) formed from two adjacent ions in the mutual dielectric displacement (x) of the ions against each other (*i.e.*, $d\mu/dx = e_{eff.}$). It has already been pointed out that the electronic polarisations can be deduced independently from the refractive indices (n). A knowledge of the refractive indices of the molecular compounds would also allow one to determine directly the part (f_i) of the total polarisation which depends on the ionic vibrations and is given by the expression of Errera and Brasseur (*Physikal. Z.*, 1933, **34**, 368) :

$$f_i = (\varepsilon - n^2)/(\varepsilon - 1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

which is free from any assumptions about the internal field.

The measurements of refractive indices were tedious. Eventually we tried a modification of Wood's method (*Phil. Mag.*, 1901, **1**, 624), briefly described in the Experimental. Although the measurements were satisfactorily reproducible, we often obtained only one or two of the refractive indices, which is probably due to a preferred orientation of the crystallites in the solid prisms. We hope to return to this in a later publication.

Another method for investigating the structure of crystalline molecular compounds would be to measure the change in the diamagnetic anisotropy occurring on the formation of the molecular compound. If one of the non-localised π-electrons is transferred, this should sometimes result in a decrease of the diamagnetic susceptibility. This was pointed out to one of us (J. W.) by Dr. Kathleen Lonsdale.

That the diamagnetic susceptibility of a molecular compound might sometimes be smaller than that of the sum of its components follows also from the above discussion for those cases where a decrease of the electronic polarisation has been observed, on the basis of the work of Kirkwood (*Physikal. Z.*, 1932, **33**, 57; see also Muller, *Proc. Roy. Soc.*, 1936, *A*, **154**, 624), who has established a relationship between polarisability and diamagnetic susceptibility. Some indication of these effects can be got from measurements by Krishnan and Banerjee (*Phil. Trans.*, 1935, **234**, 265) and Banerjee (*Z. Krist.*, 1939, *A*, **100**, 316), which are given in Table III

TABLE III.

Substance.	Mean (g.-molecular) diamagnetic susceptibility, $-\chi \times 10^6$.	Deviation, %.	Substance.	Mean (g.-molecular) diamagnetic susceptibility, $-\chi \times 10^6$.	Deviation, %.
p-Benzoquinone ...	27·0		Perylene	95·5	
Quinol	64·0		*s*-Trinitrobenzene	55·7	
	Sum : 91·0			Sum : 151·2	
Quinhydrone	92·0 } Δ = 1·0	1·1	Perylene–*s*-trinitrobenzene	142·2 } Δ = −9·0	−6·3

and show a small (positive) deviation in the case of quinhydrone (as might be expected from our own results) but a larger negative deviation in the case of the more polarisable perylene in the perylene–*s*-trinitro-molecular compound.

EXPERIMENTAL.

Preparation of Substances.—The component substances were ordinary purified specimens. Coronene was recrystallised several times from boiling benzene. Benzpyrene and methylcholanthrene were kindly supplied by Prof. J. W. Cook. Except (F) and (J), which are new, the molecular compounds (all 1 : 1) were prepared according to the following references, the letters referring to Table I : (A) Behrend, *Z. physikal. Chem.*, 1894, **15**, 186. (B) Sudborough, J., 1916, **109**, 1344. (C) Noelting and Sommerhof, *Ber.*, 1906, **39**, 77. (D) Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1938, **60**, 1665. (E) Sudborough (*loc. cit.*). (F) *Coronene–s-trinitrobenzene*, from boiling benzene, decomposes before melting (Found : N, 7·9. $C_{24}H_{12},C_6H_3O_6N_3$ requires N, 8·1%). (G) Fieser and Hershberg, *loc. cit.*, p. 945. (H) Sudborough (*loc. cit.*). (I) Noelting and Sommerhof (*loc. cit.*). (J) *Pyrene–s-trinitrobenzene*, from benzene, m. p. 248° (Found : N, 10·2. $C_{16}H_{10},C_6H_3O_6N_3$ requires N, 10·0%). (K) Cf. Siegmund, *Monatsh.*, 1909, **29**, 1091.

Measuring Cells.—The dielectric constants were measured by the change of capacity which the substances under investigation produced in the condenser-cell. The substances were available in the form of fine crystalline powders; this necessitated the use of an immersion method. The first experiments, carried out with a cell according to Eucken (*loc. cit.*), proved unsatisfactory because (i) it was difficult to obtain for the leads an absolutely tight insulating seal which was not attacked by the organic solvents used, and (ii) the brass container had a large heat capacity and a comparatively large coefficient of expansion.

A new type of cell was therefore developed : two forms of it are shown in Figs. 1*a* and 1*b*. The vessels were made of Hysil glass and parts of the inner walls were platinised, forming the electrodes. The outer electrode was kept at A.C.-earth potential. The leads were brought out through seals in the glass and terminated on two brass plates on the base. Cell 1*a* had the advantage that any small air bubble accidentally present in the liquid was well outside the electrodes when the cell was in either the upright or the inverted position. Cell 1*b* was designed for substances of which only small quantities (less that 0·1 g.) were available. The vessels were mounted on a special type of holder which enabled the cells to be turned upside-down into accurately reproducible positions. Since the total capacity of cell and holder was slightly different for either position, due to the difference in the geometrical configuration of the conductors, an adjustable, earthed, brass strip was arranged to act as an automatic trimmer, so that the total capacity was independent of the position of the cell. The leads from the holder to the oscillator were stout, bare, copper wires of about 4 mm. thickness. The connection was rigid and kept as far away from earth as possible.

Circuit (Fig. 2).—A double heterodyne method was used for measuring the change of capacity of the cell. D_1 and D_2 were two Dynatron oscillators working at about 800 kc./sec. The wave form was checked on a cathode ray oscillograph and found to be practically free from harmonics. C was a cumulative grid detector coupled extremely loosely to the oscillators, in order to prevent any reaction between the latter. With the coupling used, any small change, or further reduction of the coupling had no effect on the oscillators. T was a General Radio Company's Audio Oscillator, Type 813A, 1002 c./sec. ± 0·1%. In order to measure with sufficient accuracy the small changes of the capacity of the cell C_1, the following method was adopted : C_2 was a precision variable air condenser (linear capacity) ranging from 55 $\mu\mu$F. to 2039 $\mu\mu$F. (General Radio Company). The scale was divided into 100 parts, tenths being read by means of a vernier.

This condenser was connected in series with a small, fixed, mica condenser (C_3). By suitably choosing the value of this condenser, the measuring condenser could be made to cover the entire variation of the capacity of the cell. All the condensers were carefully shielded; hand capacity was completely absent. The changes in the measuring cell were compensated by adjustment of the precision condenser C_2.

FIG. 1*a*. FIG. 1*b*.

Condenser cells.

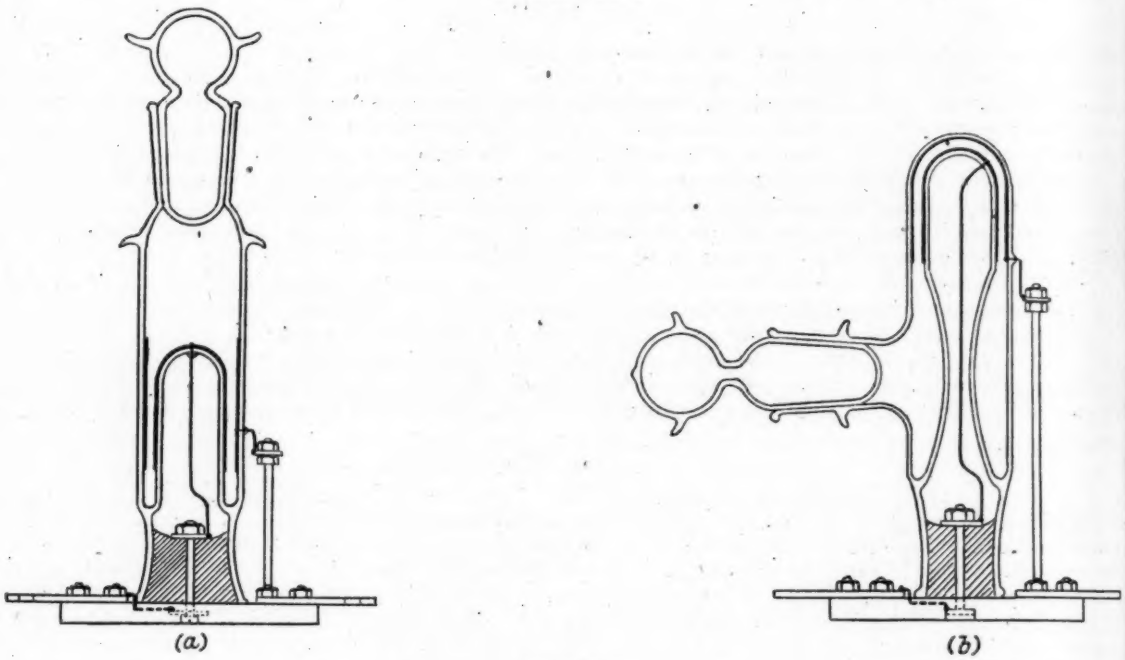
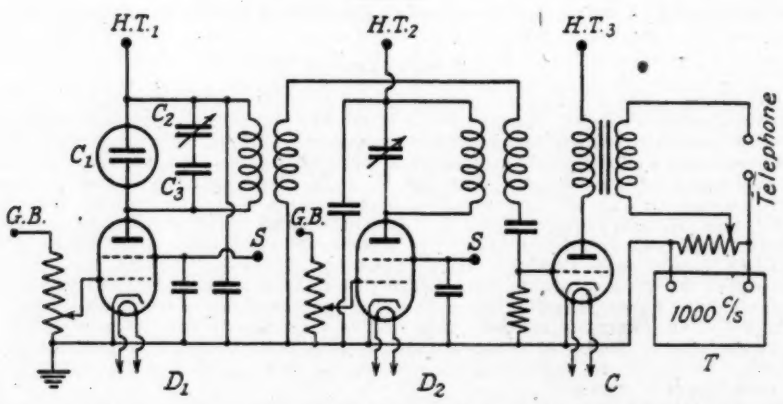


FIG. 2.



Analysis shows that any two changes Δ_1C_1 and Δ_2C_1 in the capacity of the cell and the corresponding two changes Δ_1C_2 and Δ_2C_2 in the measuring condenser are connected by the relation

$$\Delta_1C_1/\Delta_2C_1 = \Delta_1C_2[(C_2 + C_3) + \Delta_2C_2]/\Delta_2C_2[(C_2 + C_3) + \Delta_1C_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The dielectric constant ε_1 of an unknown liquid is then given by

$$(\varepsilon_1 - 1) = \Delta_1C_1(\varepsilon_2 - 1)/\Delta_2C_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

where Δ_2C_1 is the change of capacity produced by a substance of known dielectric constant ε_2. The conductivities of the solid substances and of their solutions in the immersion liquids were found to be so low that no correction had to be applied for damping. The rest of the circuit is of conventional design, care being taken to have all connections rigid. A drift of frequency due to heating of various circuit elements was eliminated by carefully heat-insulating the components involved. It was possible to keep the frequency stable to 50 cycles for long periods; the frequencies were checked, however, during and after each measurement by using one empty cell as a dummy condenser.

Procedure.—The three oscillators were switched on and left for about 1 hour before any measurements were taken. With the cell on the holder, the measuring condenser was set to a convenient value (nearly at maximum capacity) and this was taken as " zero ". The same " zero " was used for all the experiments. The second oscillator was then adjusted until the lower heterodyne note appeared and produced slow beats (5/sec.) with the tuning-fork oscillator. In order to

calibrate the instrument, *i.e.*, to determine the constant $(C_2 + C_3)$ in the above expression, two measurements were carried out with pure benzene and ethyl ether. The correctness of the value of the constant was checked on chloroform. The values of the dielectric constants used were those given by Hartshorn and Oliver (*Proc. Roy. Soc.*, 1929, *A*, **123**, 664) and Højendahl (*Z. physikal. Chem.*, 1932, *B*, **20**, 54).

In order to carry out measurements with solids, the crystalline substance was filled into the cell, so that the space between the two electrodes was approximately filled. The immersion liquids were then added. Light petroleum, ether, benzene, and nitrotoluene were found suitable, and the value obtained for the dielectric constant of any particular substance was independent of the immersion liquid. Great care had to be taken that no air was trapped by the particles or absorbed on their surface. The composition of the immersion liquid was now adjusted until its dielectric constant was the same as that of the solid. This was done by tilting the cell on the holder through 180° so that the solid dropped out of the space between the electrodes. If this did not produce any change in the frequency, the dielectric constants of the solid and of the immersion liquid were taken to be equal. At the balance position, the cell was tilted a few more times in order to ensure that a random distribution of the crystals was measured.

Measurement of Refractive Indices.—Wood's (*loc. cit.*) method was used but a simpler and more rigid type of prism was developed. It consisted of a strip of plate glass, 1 mm. thick and 1·5 cm. wide, bent to form a prism, the refracting angle lying between 3° and 6°. The substance was melted in near the refracting edge, the prism placed on a spectrometer table, and the refractive index determined in the usual way. When measuring the refracting angle, use was made of the reflections from both surfaces, in order to check the parallelism of the plate glass. Only that part of the prisms near the refracting edge was used, the rest being screened off by paper. For each substance, two measurements were made in one prism, the substance being remelted after the first measurement. The procedure was then repeated, for the same substances, with another prism of different refracting angle.

Determination of Densities.—A flotation method was used. The substances were kept under a vacuum for an appreciable time, and the immersion of the solids also took place under a vacuum.

We wish to express our sincere thanks to Prof. J. C. Prescott of the Electrical Engineering Department and to Prof. G. W. Todd of the Physics Department for the facilities which they have put at our disposal, and particularly to Mr. J. H. Smith for his help in the development and construction of the condenser cells; also to Prof. J. W. Cook, F.R.S., for the generous gift of some specimens of hydrocarbons and to Prof. C. K. Ingold, F.R.S., for his interest in this work.

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126. *The Kinetics of Aromatic Sulphonation Reactions: The Sulphonation of p-Nitrotoluene and of Chlorobenzene by Sulphur Trioxide.*

By K. D. WADSWORTH and C. N. HINSHELWOOD.

In continuation of a kinetic investigation of certain aromatic substitution reactions (see J., 1939, 1372), the sulphonations of *p*-nitrotoluene and of chlorobenzene by sulphur trioxide have been examined. Both reactions show characteristics similar to those found in the sulphonation of nitrobenzene, being of the second order with respect to sulphur trioxide and exhibiting a strong retardation due to the formation of a complex between sulphur trioxide and the sulphonic acid produced. The activation energies and log *PZ* factors found were for *p*-nitrotoluene 11,025 cals. and 4·78 respectively, and for chlorobenzene 7720 cals. and 5·14, compared with 11,400 cals. and 3·91 for nitrobenzene.

FOR many organic reactions there is a direct correlation between the effect of substituents and the activation energies of a series of reactions in which the substituent groups are varied (cf. Hinshelwood, Laidler, and Timm, J., 1938, 848). Little quantitative kinetic information is, however, available to test these correlations when applied to some of the most interesting examples of organic reactions, namely, the aromatic substitution reactions. Little kinetic investigation of the reactions has been carried out, mainly on account of the complexity of the processes involved (cf., *inter alia*, Ingold *et al.*, J., 1927, 2918; 1931, 1959,; 1938, 905, 918, 929).

Vicary and Hinshelwood (J., 1939, 1372), however, found that the sulphonation of nitrobenzene by sulphur trioxide was reasonably amenable to kinetic study. Nitrobenzene was both reactant and solvent, the reaction being followed at several temperatures in the range 25—100° by the change in acidity as dibasic sulphur trioxide is converted into monobasic sulphonic acid: $C_6H_5{\cdot}NO_2 + SO_3 \longrightarrow NO_2{\cdot}C_6H_4{\cdot}SO_3H$.

The reaction: (1) was of second order with respect to sulphur trioxide, (2) exhibited a marked retardation ascribable to the formation of a 1 : 1 complex between the product and sulphur trioxide, and (3) was little influenced by sulphuric acid at higher temperatures, though retarded by it at lower temperatures.

The second order of the reaction with respect to sulphur trioxide shows that it must proceed by a mechanism involving either (*a*) S_2O_6 molecules in equilibrium in small amount with SO_3 molecules, or (*b*) two SO_3 molecules. It is not known whether the dimer is in fact present to any appreciable extent in dilute solutions in nitrobenzene, though Michael and Weiner (*J. Amer. Chem. Soc.*, 1936, **58**, 294) present evidence of certain preparative reactions, indicating that S_2O_6 is the active agent in sulphonations. If the mechanism involved two trioxide molecules, the second molecule might (i) enter into some relation with the nitro-group which enhances the activity of the benzene nucleus, or (ii) act, in a manner analogous to a basic catalyst, by providing a temporary home for proton replaced from the C–H bond by the first sulphur trioxide molecule.

The various possibilities can only be resolved by the study of further aromatic compounds, with and without substituent nitro-groups. In the present work we have examined the sulphonation by sulphur trioxide of *p*-nitrotoluene and of chlorobenzene. Since both the compounds studied are sulphonated more rapidly than nitrobenzene, this was used as solvent, in order to ensure that the medium conditions were as near as possible to those of the nitrobenzene–sulphur trioxide reaction. In the latter the aromatic reactant was present in large excess and this condition is now only approximately fulfilled.

The reactions were started by mixing measured volumes of the aromatic reactant solution and a freshly prepared sulphur trioxide solution, both preheated to the requisite temperature. After the desired time interval, the reaction was stopped by pouring the reaction mixture into water and shaking vigorously. The extent of the change was determined by titration with alkali.

The error introduced by reaction between nitrobenzene and sulphur trioxide during the preheating was small at the lower temperatures but was appreciable at 60° and a correction was applied. The initial rates measured from the "percentage change"–time curves were also corrected for the simultaneous nitrobenzene–sulphur trioxide reaction.

Sulphone formation, which would also lead to a 50% titre drop, $2C_6H_6 + 2SO_3 \longrightarrow (C_6H_5)_2SO_2 + H_2SO_4$, gives sulphuric acid, which was determined gravimetrically in the end-products.

The reactions consistently show retardation by their products, which can be explained by the removal of sulphur trioxide in the formation of a 1 : 1 complex with the sulphonic acid.

Experimental.

Nitrobenzene was dried over calcium chloride for several weeks and then distilled. The middle fraction was redistilled at 207—209°.

p-Nitrotoluene was recrystallised from light petroleum until a product melting sharply at 54° was obtained. This was dissolved in nitrobenzene in proportions necessary for a 3M-solution.

Chlorobenzene was dried over calcium chloride and distilled several times. It was then mixed with nitrobenzene to give a 0·5M-solution. (The rate of sulphonation is considerably greater than that of *p*-nitrotoluene, and for a measurable rate it is necessary to use a less concentrated solution.)

Sulphur trioxide in nitrobenzene was freshly prepared for each experiment, from 65% fuming sulphuric acid. This was usually done by heating the oleum to 60—70° and passing a stream of dry air over the surface. The sulphur trioxide carried over was collected in nitrobenzene, an all-glass apparatus being used. This method gave solutions containing less sulphuric acid than those obtained by the method of Vicary and Hinshelwood.

For 15°, 25°, 40°, and 60°, electrically heated water- or oil-baths were used. The measurements at 0° were carried out in a Dewar vessel filled with melting ice. The end-point measurements were made at 120° in an oil-bath heated by boiling perchloroethylene (b. p. 121·2°). Thermometers were calibrated against N.P.L. standards.

Three different arrangements for preheating and mixing the reactants and for stopping the reaction were used according to the rate to be measured. They were:

1. 2-C.c. portions of the aromatic reactant were pipetted into tubes of about 5—10 c.c. capacity. These were then placed in the thermostat together with the bottle containing freshly-prepared sulphur trioxide solution. After time had been allowed for thermal equilibrium to be established, 2-c.c. portions of the sulphur trioxide solution were pipetted into the reaction tubes, which were closed with rubber caps, and a further 2-c.c. portion was run into water in order to determine the initial titre. The reaction was stopped by rapidly pouring the contents of the tube into water, shaking vigorously, and washing out the reaction tube. This method was used for all reaction times greater than about 2½ minutes.

2. 2-C.c. portions of the reactant solutions were pipetted into the separate limbs of an inverted Y-tube placed in he thermostat. After a suitable interval, the reactant solutions were mixed by tipping the tube, so that the solutions ran from limb to limb. The reaction was stopped as in (1) above. The initial titre in these runs was found by placing a tube containing 2 c.c. of sulphur trioxide solution in the thermostat for the same length of time as was required for preheating. This method was used for reaction times between ½ and 2½ minutes.

3. A pair of tubes, the ends of which were blown into bulbs, and which fitted one inside the other, was used. These tubes were carried in a cork fitting tightly into a boiling-tube which contained water. The chlorobenzene solution was pipetted into the outer tube and the sulphur trioxide solution into the inner tube, which was closed by a rubber cap. The reactants could be mixed by breaking the bulb of the inner tube with a glass rod. The reaction could be stopped by breaking the second bulb in a similar manner and shaking the reaction mixture vigorously with the water. The initial titre was determined in the same way as in (2) above. This method was used for all reaction times less than ½ minute.

Titrations were made with N/20-alkali and methyl-red, the end-point being determined by adding excess alkali, shaking vigorously, back-titrating with N/20-hydrochloric acid, and repeating until successive additions of acid and alkali were equivalent.

For reaction end-points, 2 c.c. were heated at 120° for 24 hours. The dark colour made it impossible to use methyl-red, but bromothymol-blue proved satisfactory.

Investigation of Sulphone Formation.—Formation of sulphone is accompanied by the production of an equivalent amount of sulphuric acid. Initially the solutions contain sulphuric acid in an amount which is given by (Initial Titre − 2 × Titre Drop), and when gravimetric analysis of the end-point products reveals sulphuric acid appreciably in excess of this, the discrepancy is due to sulphone formation. 5-C.c. portions of each reactant solution were sealed off and heated at 120° for two days. The product was extracted with water and with benzene, the nitrobenzene dissolving in the benzene and the sulphuric and sulphonic acids in the water. The benzene layer was washed several times with water and with alkali. The combined aqueous layer was concentrated to about 100 ml., and the sulphuric acid determined by precipitation as barium sulphate.

Correction to the Initial Sulphur Trioxide Concentrations in Runs at 60°.—Suppose the initial titre before preheating is a ml., and that after preheating is b ml. Now:

$$Ar{\cdot}H + SO_3 \longrightarrow Ar{\cdot}SO_3H \text{ and } Ar{\cdot}SO_3H + SO_3 \rightleftharpoons [Ar{\cdot}SO_3H,SO_3] \xrightarrow{\text{water}} Ar{\cdot}SO_3H + H_2SO_4$$

Hence the amount of sulphur trioxide used up by reaction with nitrobenzene during preheating is equivalent to $2(a - b)$ ml. titre. Since we may assume that complex formation is complete at the large initial sulphur trioxide concentrations, the amount of trioxide used in complex formation is equivalent to $2(a - b)$ ml. titre also. Hence the "effective" initial titre is $\{a - 4(a - b)\}$ ml. As the complex breaks up in water, its formation will not affect titres during the course of the runs and the titre fall is given by $\{a - (a - b)\} - x$, *i.e.*, $(b - x)$ ml., where x is the particular titre concerned.

Results.—(a) *The order of the reaction, the velocity constants, and the activation energy.* The extent of reaction was expressed in terms of percentage change, and plotted against time. Initial rates were determined from the reaction curves, by drawing the tangent at the origin, and were corrected where necessary for the simultaneous nitrobenzene reaction.

The values of the initial rates found with *p*-nitrotoluene at 25° and with chlorobenzene at 15° are shown in Table I.

TABLE I.

Initial Rates and Sulphur Trioxide Concentrations.

p-*Nitrotoluene at* 24·91°.

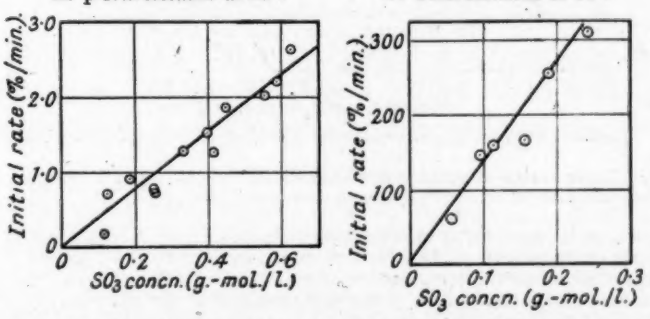
SO_3 concn., g.-mol./l.	Initial rate (%/m.).	Nitrobenzene initial rate (%/m.).	Corrected initial rate (%/m.).	SO_3 concn., g.-mol./l.	Initial rate (%/m.).	Nitrobenzene initial rate (%/m.).	Corrected initial rate (%/m.).
0·394	1·620	0·078	1·542	0·446	1·940	0·088	1·852
0·187	0·945	0·035	0·910	0·125	0·737	0·025	0·712
0·251	0·815	0·049	0·766	0·254	0·780	0·050	0·730
0·551	2·150	0·109	2·041	0·585	2·340	0·116	2·224
0·332	1·360	0·066	1·294	0·112	0·202	0·022	0·180
0·412	1·350	0·082	1·268	0·622	2·770	0·123	2·647

Chlorobenzene at 14·91°.

SO_3 concn., g.-mol./l.	0·096	0·156	0·189	0·114	0·056	0·241
Initial rate (%/m.)	148·0	166·4	256·0	160·4	62·5	310·4

FIG. 1.

A. p-*Nitrotoluene at* 25°. B. *Chlorobenzene at* 15°.



Plots of the initial rates (in %/min.) against the sulphur trioxide concentration (see Figs. 1, A and B) give fair straight lines passing through the origin, thus demonstrating the second-order nature of the reaction with respect to sulphur trioxide. From the slopes of such lines we obtain the reaction velocity constants given in Table II.

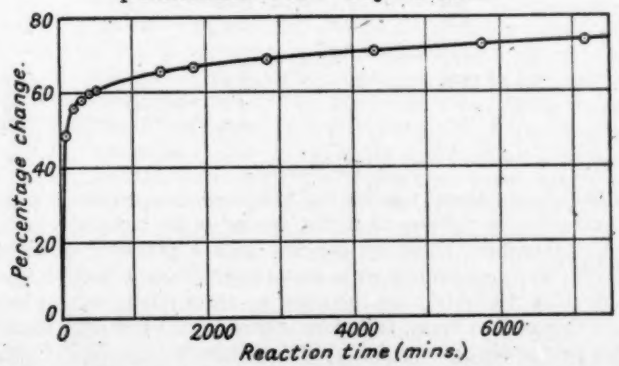
TABLE II.

Reaction Velocity Constants at Different Temperatures.

p-*Nitrotoluene.*		*Chlorobenzene.*	
Temp.	Mean $k \times 10^5$ (l./g.-mol. sec.).	Temp.	Mean k (l./g.-mol. sec.).
0·0°	9·2	0·0°	0·102
14·9	31·8	14·9	0·216
24·9	62·3	24·9	0·369
39·9	143	39·9	0·600
60·0	354		

FIG. 2.

p-*Nitrotoluene at* 40°. $SO_3 = 0·351$ M.



By application of the Arrhenius equation, the following values of the activation energies and non-exponential factors were calculated :

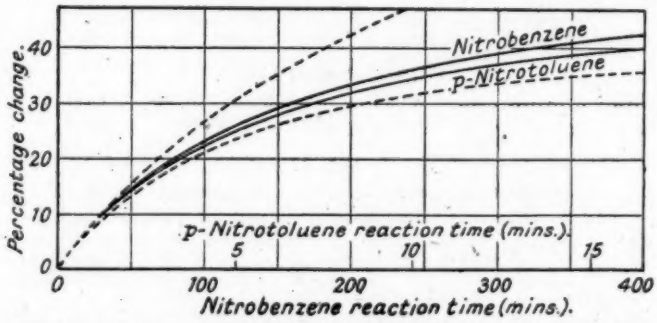
	p-Nitrotoluene.	Chlorobenzene.	Nitrobenzene (Vicary and Hinshelwood).
E (cals.)	11,025	7720	11,400
$\log_{10} PZ$	4·79	5·14	3·91

(b) *The retardation of the reaction.* The reaction curves in Fig. 2 show that the reaction rate falls off as the reaction

proceeds. Thus in the *p*-nitrotoluene reaction, only a little more than 50% reaction has occurred after 3 days and in the fourth day the reaction proceeded only another 4% towards completion. Vicary and Hinshelwood found the same characteristic in the nitrobenzene sulphonation and showed that it was explainable by the formation of a 1 : 1 complex between the sulphonic acid and sulphur trioxide. In the later stages, the reaction will be controlled by the concentration of trioxide in equilibrium with the complex. From the rates of the reaction at different stages, Vicary and Hinshelwood determined the ratios " Free SO_3/Total SO_3 " throughout the reaction and so were able to calculate velocity constants from the later course as well as from the initial rates of the reaction.

With *p*-nitrotoluene, the complex appears to be formed somewhat more completely than with nitrobenzene, as is shown by Fig. 3, in which a nitrobenzene and a *p*-nitrotoluene run at 40° have been compared on an adjusted time scale.

FIG. 3.



Broken curves :—upper 0%, *lower* 100% *of* 1 : 1*-complex formation.*

(c) *Sulphone formation.* Table III gives some typical results of the gravimetric analyses for sulphuric acid. In the *p*-nitrotoluene reaction, these determinations were made on end-point products at 120°, and it is seen that sulphone formation is unimportant.

With chlorobenzene, however, it seemed that appreciable sulphone formation took place at temperatures considerably lower than 120°, and therefore analyses were made on end-point products at 15°, 25°, and 40°. In general, the proportion of sulphone formed tended to fall off as the temperature of reaction increased, but the results were irregular and very possibly vitiated by some uncontrollable hydrolysis of the sulphonic acid in the analysis.

TABLE III.

Sulphone Formation : Results of Gravimetric Analyses. (*All data are in terms of ml. of* N/20.)

			p-Nitrotoluene.				
Initial titre	79·5	81·0	26·5	51·8	22·0	124·2	100·5
Initial titre −2 × titre drop	14·5	9·6	6·6	11·2	4·1	14·7	12·3
Equiv. of $BaSO_4$ found	13·8	9·3	7·5	11·1	5·9	10·0	10·2
			Chlorobenzene.				
			At 15°.				
Initial titre	30·6	19·0	28·1	33·8	22·2	12·2	41·6
Initial titre −2 × titre drop	2·5	3·6	3·2	3·5	3·9	3·2	3·1
Equiv. of $BaSO_4$ found	7·0	5·1	8·7	7·9	5·5	4·4	5·3
			At 25°.				
Initial titre	24·1	36·5	20·9	37·0	11·9		
Initial titre −2 × titre drop	2·9	4·1	3·7	4·8	5·1		
Equiv. of $BaSO_4$ found	9·1	7·3	4·4	11·2	3·7		
			At 40°.				
Initial titre	11·3	23·1	22·4	38·3	18·3	39·5	
Initial titre −2 × titre drop	5·5	4·3	4·3	5·6	5·1	5·0	
Equiv. of $BaSO_4$ found	3·1	5·5	5·0	11·5	4·3	4·5	

DISCUSSION.

Since the sulphonation of chlorobenzene, like that of the nitro-compounds, depends on the second power of the sulphur trioxide concentration, it follows that the second-order reaction does not arise from a specific property of the nitro-group. It might, however, depend upon a property of all strongly polar substituent groups. If the bimolecularity were connected with some interaction, possibly of a dipolar nature, between sulphur trioxide and the substituent group, then the chlorine atom might behave similarly to the nitro-group. The problem of the detailed mechanism must, therefore, remain unsolved until data for benzene or derivatives containing no strongly polar substituent groups have been obtained.

Apart from possible doubts about the inherent unlikelihood, under the conditions prevailing, of S_2O_6 as the active species, the scheme $2SO_3 \rightleftharpoons S_2O_6$; $ArH + S_2O_6 \longrightarrow Ar{\cdot}S_2O_6H$; $Ar{\cdot}S_2O_6H \rightleftharpoons Ar{\cdot}SO_3H + SO_3$ is attractive, since it would explain both the second order with respect to SO_3 and also the retardation of the reaction as it proceeds.

Turning to the kinetic and electronic aspects, it appears that the values calculated for the probability factor, *P*, do not differ very greatly for the three reactions. The value of the collision frequency, *Z*, required

for these calculations, was estimated on the assumption that whenever two sulphur trioxide molecules meet there will be a molecule of the aromatic reactant suitably disposed for reaction. This assumption is probably quite justified for the nitrobenzene and the *p*-nitrotoluene reaction, where there are respectively a large excess and a moderate excess of aromatic reactant, but it is not strictly true under the conditions used for chlorobenzene. This will make the estimate of Z for the latter somewhat too large and hence the value of P rather too small. The values of P, and of E, are :

	E, cals.	P.
Nitrobenzene	11,400	$1{\cdot}9 \times 10^{-7}$
p-Nitrotoluene	11,025	$1{\cdot}65 \times 10^{-6}$
Chlorobenzene	7,720	$3{\cdot}2 \times 10^{-4}$

It appears then that the conditions under which the molecules react in the three reactions are not very different. The very much greater rate of the chlorobenzene sulphonation is clearly associated with a considerably smaller activation energy rather than with an increased reaction probability. With *p*-nitrotoluene, which contains an activating and a deactivating group, it appears that it is the latter which determines the reactivity, since the activation energy is little different from that for nitrobenzene.

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127. *Analysis of Mixtures of 2 : 3 : 4 : 6-Tetramethyl Glucose with 2 : 3 : 6-Trimethyl and Dimethyl Glucoses by Partition on a Silica–Water Column : A Small-scale Method for Investigating the Structures of Glucopolysaccharides.*

By D. J. BELL.

By using a method of partition between organic solvents and water held in a column of silica gel, amounts of 50—200 mg. of 2 : 3 : 4 : 6-tetramethyl glucose can be quantitatively separated from 2 : 3 : 6-trimethyl glucose present in 1—200 molecular proportions. Separation of dimethyl glucoses from the tri- and tetra-methyl sugars can also be effected. The method is thus suitable for the investigation of relatively small amounts of the appropriate polysaccharides. The results of analyses of specimens of methylated glycogens and whole starch show that, with respect to end-group assay, the accuracy of the method is comparable with the distillation procedure. Isolation and estimation of the dimethyl glucose fractions are greatly facilitated. Clear-cut separation of sugars is obtained without the complication of mixed fractions.

At present the structure of oligo- and poly-saccharides is best investigated by analysis of the hydrolysis or methanolysis products of the methylated substances. Haworth, Hirst, and others have developed the methods of Purdie and of Irvine to produce the gravimetric method of " end-group assay " based on the fractional distillation of the methylated constituent radicals in the form of their methylglycosides (Haworth and Machemer, J., 1932, 2270; Hirst and Young, J., 1938, 1247; Peat and Averill, J., 1938, 1244; Peat and Whetstone, J., 1940, 276). Such analyses have often revealed the existence of " unit-chains " of monosaccharide radicals, each terminating in a characteristic " end-group." Furthermore, evidence has been obtained for the presence of certain radicals apparently concerned in glycosidic links between adjacent unit chains in such a manner that the whole assemblage or macromolecule possesses, in Haworth's term, a " laminated " structure.

Provided sufficient material be available, end-group assay is accurate with respect to the determination of actual terminal radicals, *e.g.*, tetramethyl methylhexosides terminating unbranched unit chains of hexose radicals. The method suffers from two disadvantages. First, by fractional distillation it is impossible quantitatively to obtain absolute separation of a higher from a lower methylated glycoside *; mixed fractions can, however, be handled with reasonable accuracy, as Hirst and Young (*loc. cit.*) have shown in the case of 2 : 3 : 4 : 6-tetramethyl and 2 : 3 : 6-trimethyl methylglucosides (see also Bacon, Baldwin, and Bell, *Biochem. J.*, 1944, **38**, 198). The second and more serious drawback is the tendency of partly methylated sugars, during the preparation of their methylglycosides, to undergo autocondensation and demethylation to an extent at present unpredictable. This introduces uncertainty into the assay of non-terminal radicals. Such is certainly the case with polysaccharides of the amylose, amylopectin, and glycogen types, where estimation of the dimethyl glucose radicals, which occur in only small proportion, affords important evidence in favour of a laminated aggregation of unit chains (cf. Freudenberg and Boppel, *Ber.*, 1940, **73**, 609).

We desired to estimate not only the end-groups, but also the radicals which yield dimethyl glucoses, in polysaccharides of the above-mentioned types. To avoid the complicating feature of autocondensation we considered the problem of separating the free methylated sugars. Macdonald (*J. Amer. Chem. Soc.*, 1935, **57**, 771) has shown that the partition coefficients of 2 : 3 : 4 : 6-tetramethyl and 2 : 3 : 6-trimethyl glucoses differ by a factor of 100, thus allowing quantitative separation of the two sugars by customary partition procedure. The manipulations involved, however, are unsuitable for the small quantities we desired to estimate, although for amounts of the order of grams, simple partition methods are practicable for assaying 2 : 3 : 4 : 6-tetramethyl glucose, and have in fact been used to estimate unit-chain lengths (Bell, *Biochem. J.*, 1935, **29**, 2031; 1936, **30**, 1612; Hassid and Dore, *J. Amer. Chem. Soc.*, 1937, **59**, 1503). By partitioning between chloroform and water held in the form of a rigid column by means of silica gel, we have achieved, on a small scale, absolute separation of

* See, however, Levi, Hawkins, and Hibbert, *J. Amer. Chem. Soc.*, 1942, **64**, 1957.

2 : 3 : 4 : 6-tetramethyl and 2 : 3 : 6-trimethyl glucoses. The procedure is analogous to the method of partition chromatography used by Gordon, Martin, and Synge for the separation of acetamido-acids (*Biochem. J.*, 1941, **35**, 1388; 1943, **37**, 79), and applied by Elsden (*Biochem. J.*, in the press) to the separation of short-chain fatty acids (cf. Smith, *Biochem. J.*, 1942, **36**, xxii).

We have further achieved the separation of trimethyl from dimethyl glucoses by partitioning between the silica–water column and a mixture of chloroform with one-tenth of its volume of *n*-butanol. This mixed solvent extracts from water nearly 12 times as much 2 : 3 : 6-trimethyl glucose as does chloroform alone. In both separations the individual sugars are recovered in high yield and analytically pure within the limitations of the methods employed.

The operations are simple and reliable, provided the precautions detailed below be adopted. Using artificial mixtures of known composition, we have been able to assay 2 : 3 : 4 : 6-tetramethyl glucose in amounts ranging from 50 to 200 mg. in the presence of 1—200 molecules of 2 : 3 : 6-trimethyl glucose. The method has further been successfully tested on methylated derivatives of cellobiose, glycogen, and whole starch. The actual materials had all been previously analysed on a large scale by the distillation method. Results are shown in the following table. Roman numerals indicate: (I) results obtained by the partition method, (II) results obtained by the fractional distillation procedure.

Substance.	Methylated cellobiose.	Methylated glycogen (horse muscle).	Methylated glycogen (*Ascaris*).	Methylated whole starch (rice).	
Weight analysed (g.)	0·1600	1·124	0·9824	3·120	1·539
Number of radicals, to each "end-group":					
"Trimethyl" (I)	1·00	8·95	12·4	21·2	22·6
(II)	1·00	8 ·	12·7	28·1 *	
"Dimethyl" (I)	—	2·05	1·7	4·5	4·5
(II)	—	1·9	0·8	*	
Total number of radicals in average unit-chain: (I)	2	12	15	26—28	
(II)	2	12	13—14	29	

* The non-terminal radicals were estimated together as one fraction.

Experimental.

Obligatory Precautions.—(*a*) Apparatus must be free from grease; stop-cocks may be lubricated with graphite. (*b*) Organic solvents must be distilled from all-glass apparatus; chloroform is thoroughly washed with water before distillation and may conveniently be stored in a large separating funnel, under a layer of water. (*c*) Care must be taken to free substances for analysis from all traces of organic contaminants of low volatility, such as acetone condensation products. (*d*) To guard against autocondensation of sugars, all chloroform solutions must be evaporated in the presence of small amounts of barium carbonate (cf. Purdie and Irvine, J., 1905, **87**, 1022).

Preparation of the Silica.—The instructions of Gordon, Martin, and Synge (*loc. cit.*, 1943) must be strictly followed, but addition of indicator to the silica is omitted. Prolongation of the period stated for "ageing," or delay in completing the washing of the aged material, enhances the absorptive properties of the silica and thus hinders rapid partition.

Preparation of the Silica–Water Column.—One part of dry silica is ground (draught cupboard) in a mortar, and one-half of its weight of water stirred into the powder with further grinding to ensure efficient mixing. A glass tube, of dimensions appropriate to the operation (see below), is loosely plugged at one end by cotton-wool resting on a removable, perforated, porcelain disc. The moist silica is made into a slurry with chloroform and poured into the tube. The gel rapidly packs into a column on top of the plug. The supernatant chloroform is allowed to drain through the gel and the column is then degreased by running through two "column-lengths" of chloroform, one after the other. The apparatus is then ready for use.

Testing the Rate of Partition of the Column.—Different batches of silica show variations in absorptive properties. We therefore carry out an empirical test on each batch. Three columns, each of 2·5 g. of silica, are prepared in tubes of 10 mm. diameter; degreasing is not necessary. One ml. each of chloroform solutions (1 mg./ml.) of 2 : 3 : 4 : 6-tetramethyl and 2 : 3 : 6-trimethyl glucoses are carefully pipetted on to the surface of each column and the liquid allowed to sink in. One column-length of chloroform is then allowed to pass through each column. One tube is now ready for examination. The second tube is then treated with four column-lengths of chloroform, and the third tube held in reserve. The first and the second column are now expressed from the tubes by placing a glass-rod against the base-plug and smoothly drawing the tube back, over the plug, so as to leave the extruded column lying on a glass or porcelain plate. The gel is then dried at 110° and allowed to cool. Fine drops of 2% alcoholic α-naphthol are then applied at regular intervals along the length of the dried columns, followed by similar "spotting" with concentrated sulphuric acid. A deep mauve coloration (Mölisch reaction) indicates the areas occupied by the sugars, obvious threads of cellulose being disregarded. Both columns will show a pronounced band at the top (trimethyl sugar), and the first should show a second band (tetramethyl sugar) near the base, with little or no "tailing." If the silica is "good" (low absorption), the second column will show only the trimethyl band, for all the tetramethyl glucose will have been eluted. Should the second column still retain tetramethyl sugar, the reserve column should be treated with eight column lengths and examined as before. If, in its turn, this column still retains tetramethyl glucose, the batch of silica must be rejected. As the relative rates of movement on the column of the two sugars differ so greatly, complete separation is easily accomplished.

Procedure for Hydrolysis of Methylated Glucopolysaccharides.—The following procedure has given satisfactory results with derivatives of polysaccharides linked between positions 1 and 4 in both α- and β-orientations. Hydrolysis must be complete; if it is not, oligosaccharides will appear in the "tetramethyl fraction." The substance, dissolved in a mixture of 5 parts of glacial acetic acid with 10 parts of 5% (w/v) hydrochloric acid, is heated for 5 hours on the boiling water-bath. After cooling a slight excess of saturated lead acetate is added, and the precipitate of lead chloride filtered off and washed with a little ice-water. Hydrogen sulphide is passed through the filtrate and washings to precipitate lead ions, lead sulphide is filtered off, and the colourless solution, with frequent additions of water, is distilled in a vacuum below 50° to remove acetic acid. The solution must not be evaporated to dryness, as condensation between sugar molecules is catalysed by traces of acid. Chloride ions are removed from the acetic acid-free solution by addition of silver carbonate, followed by filtration and precipitation of colloidal silver from the filtrate by hydrogen sulphide. After

filtration through kieselguhr, the solution may be either evaporated to dryness in a vacuum, or directly used for analysis as described in the following section.

Analysis of the Hydrolysate.—The following sequence of operations covers a wide range of possibilities.

(I) An amount of the hydrolysate containing 100—200 mg. of tetramethyl glucose dissolved in 10—15 parts of water is filtered through charcoal into a graduated separating-funnel, and the final concentration brought to approximately 5% by water washings. The solution is shaken nine times with its own volume of chloroform, and the latter evaporated, without dehydration, at ordinary pressure. The extract contains all the tetramethyl glucose, and, in addition, about 10% of the trimethyl sugar of the hydrolysate. If the amount of the latter sugar extracted is suspected to exceed 300 mg., a second partition, similar to the first, must be carried out, in order not to overload the column.

(II) The sugars, extracted in (I), are dissolved in chloroform and quantitatively transferred by pipette to a column prepared from 25 g. of silica in a tube of 40 mm. diameter. When the solution has completely entered the column, the tetramethyl glucose is eluted by passage of the requisite number of column-lengths of chloroform. This number is determined by the routine test on the batch of silica used, with the addition of two column-lengths to provide a factor of safety. A good silica thus requires 5 + 2 = 7 column-lengths, whereas poor material requires 9 + 2 = 11. The eluate is evaporated, and dried for an hour by means of the water pump over sulphuric acid and solid sodium hydroxide.

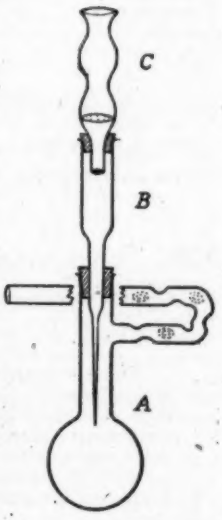
(III) The tetramethyl glucose from (II), dissolved in light petroleum–dry ether (3 : 1), is pipetted into the evaporation apparatus (see below). The residual sugar is dried to constant weight at the vacuum of the water pump.

(IV) The aqueous phase from (I) is shaken with an equal volume of chloroform–butanol (9 : 1). This extracts approximately 15% of the trimethyl sugar present. The process is repeated until not more than 500 mg. of the latter remain in the aqueous phase, which is then evaporated to dryness under reduced pressure. The residual sugars are dissolved in the chloroform–butanol mixture, and pipetted on to the same column as before. The trimethyl glucose is eluted by chloroform–butanol, the number of column-lengths required being the same as that employed in (II).

(V) The chloroform–butanol solutions from (IV) are united and evaporated to dryness, water being added to assist the removal of the butanol, under reduced pressure. The residual trimethyl glucose is dissolved in ether–acetone (2 : 1), the solution made up to a definite volume, and an aliquot, corresponding to about 1 g. of sugar, concentrated in the evaporation apparatus. The sample is dried to constant weight in a high vacuum.

(VI) The column is expressed from the tube, and the dimethyl sugar (and any traces of lower homologues) extracted by washing the gel five times with 100-ml. lots of acetone. The resulting solution is evaporated to dryness, and the residue, dissolved in warm, dry ethyl acetate, transferred to the evaporation apparatus and finally dried to constant weight in a high vacuum.

The Evaporation Apparatus (see Fig.).—This consists of three parts. *A* is a small flask of about 5 ml. bulb capacity. A side tube inserted in the neck is bent upwards and backwards though an angle of 180° and is " dimpled " at intervals to provide baffles. *B* is an adapter with the narrow limb drawn into a capillary which reaches just into the bulb of *A*. *C* is a small sintered-glass filter (G4). On the filter disc is packed a 2-mm. layer of barium carbonate covered by a further 2-mm. layer of charcoal. These absorbents remove traces of impurities from the sugar solutions. After being weighed, *A* is attached to *B* and *C* and warmed in a small air-bath at 70—80°. Gentle suction is applied to the side limb of *A* by a water pump (manometer about 730 mm. Hg), and the solution to be evaporated is pipetted, in small portions, through *C*. Excessive spurting in *A* must be regulated by the length and bore of the capillary of *B* and by choosing a suitable degree of vacuum. When the solution and necessary washings have been evaporated to a syrup, which may crystallise spontaneously, the inside of the adapter and the outside of the capillary are washed with a few drops of dry acetone. Solvents remaining in *A* are removed by applying full vacuum for 5 minutes. *A* and its contents are then dried to constant weight in a vacuum desiccator over sulphuric acid and solid sodium hydroxide.



Typical Recovery Experiments upon Artificial Mixtures.—(i) A mixture of 183 mg. of tetramethyl and 114 mg. of 2 : 3 : 6-trimethyl glucose was dissolved in chloroform and analysed on a column of " good " silica. The chloroform eluate yielded 171 mg. of tetramethyl glucose (93%), and the chloroform–butanol eluate yielded 107 mg. (92%) of the trimethyl sugar. Both sugars were recovered in analytically pure condition.

(ii) 147 Mg. of tetramethyl glucose and 102 mg. of trimethyl glucose were analysed on a column of " poor " silica; 138 mg. (93%) and 94 mg. (92%) were the respective amounts of the two sugars recovered analytically pure.

(iii) A mixture composed of 58·6 mg. (1 mol.) of tetramethyl and 11,220 mg. (200 mols.) was subjected to the complete processes of hydrolytic and partition treatments before being analysed on the column. The two sugars were recovered in respective amounts of 50·0 mg. (86%) and 10,550 mg. (94%), *i.e.*, 1 : 224 mols.

(iv) Experiments with dimethyl glucoses gave recoveries of the same high order.

Analysis of Heptamethyl β-Methylcellobioside.—160 Mg. were hydrolysed, yielding 145·5 mg. of mixed sugars (approx. 90% recovery). Separation on the column yielded: (*a*) crystalline 2 : 3 : 4 : 6-tetramethyl glucose, 71 mg. (95%) (Found: OMe, 52·3. Calc.: OMe, 52·5%), $[\alpha]_D$ (water) +82·5°; (*b*) crystalline 2 : 3 : 6-trimethylglucose, 66·0 mg. (94%) (Found: OMe, 41·4. Calc.: OMe, 41·9%), $[\alpha]_D$ (water) +70°. The two sugars were thus recovered in equimolecular proportion.

Simple End-group Assay on Methylated Glycogen (Horse Muscle).—The material used (OMe, 44·7%) was the actual sample shown by the distillation method to have a unit chain length of 11—12 radicals (Bell, *Biochem. J.*, 1937, **31**, 1683). 2013 Mg. were hydrolysed, yielding 2000 mg. of mixed sugars (approx. 92% recovery), which were dissolved in water and the volume made up to 50 ml. The solution was divided into two portions for separate analyses on the silica–water column. (*a*) Analysis of 1000 mg. of the mixed sugars yielded 78·8 mg. of crystalline tetramethyl glucose (Found: OMe, 52·1%), $[\alpha]_D$ (water) +83°; after allowance for a 6% loss on column working, this corresponds to an end-group percentage of 8·4, *i.e.*, a unit-chain length of 11—13 radicals. (*b*) 940 Mg. of mixed sugars yielded 77 mg. of crystalline tetramethyl glucose (Found: OMe, 52·1%), $[\alpha]_D$ (water) +80°, again corresponding to a unit-chain length of 11—13 radicals.

Complete Analysis of Glycogen (Horse Muscle).—1124 Mg. of the same material as that used in the above experiments yielded, after hydrolysis, 1128 mg. of mixed sugars (recovery, approx. 93%). Analysis on the column gave the following results:

Methylated sugar.	Found, mg.	OMe, %.	$[\alpha]_D$ (water).	Molecular ratio.
Tetramethyl	93	52·1	+80°	1
Trimethyl	783	41·7	+70	8·95
Dimethyl	168	28·2	—	2·05

Unit-chain has average length of 12 radicals.

Complete Analysis of Glycogen (Ascaris lumbricoides).—The material used was the actual sample of methylated glycogen analysed by the distillation method by Baldwin and King (*Biochem., J.*, 1942, **36**, 37), in this laboratory, and found to have a unit-chain length of 13—14 radicals. 982·5 Mg. of material yielded 980·4 mg. of hydrolysis products (recovery, approx. 93%). Analysis on the column gave the following results:

Methylated sugar.	Found, mg.	OMe, %.	$[\alpha]_D$ (water).	Molecular ratio.
Tetramethyl	63	52·5	+83°	1
Trimethyl	748	41·7	+71	12·4
Dimethyl	96	29·8	—	1·7

Unit-chain has average length of 15—16 radicals.

Complete Analysis of Whole Rice Starch.—A commercial sample was methylated directly (Peat and Whetstone, *loc. cit.*) until a methoxyl content of 43·1% was attained. The sample displayed the expected physical properties, and in aqueous solution gave an intense blue with iodine–potassium iodide solution. The analysis was performed in duplicate, with the results shown below.

(i) 3120 Mg. gave 3225 mg. of hydrolysis products (recovery, approx. 95%).
(ii) 1539 Mg. gave 1437 mg. hydrolysis products (recovery, approx. 88%).

Methylated sugar.	Found, mg. (i).	Found, mg. (ii).	OMe, %. (i).	OMe, %. (ii).	$[\alpha]_D$ (water). (i).	$[\alpha]_D$ (water). (ii).	Molecular ratio. (i).	Molecular ratio. (ii).
Tetramethyl	121	52	52·3	52·0	+84°	+82°	1	1
Trimethyl	2398	1104	41·6	41·5	+69	+70	21·1	22·6
Dimethyl	481	207	29·2	30·0	—	—	4·5	4·5

Unit-chain length has average length of 26—28 radicals.

The author is indebted to Professor A. C. Chibnall, F.R.S., for his interest and encouragement, and to Drs. E. Baldwin, S. R. Elsden, R. L. M. Synge, and G. R. Tristram for helpful discussions. Financial assistance from Messrs. Imperial Chemical Industries Ltd. is gratefully acknowledged.

THE BIOCHEMICAL LABORATORY, CAMBRIDGE. [*Received, July 24th*, 1944.]

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128. *Experiments on the Synthesis of Purine Nucleosides. Part VII. Some Further Observations on the Synthesis of Pyrimidines from Esters and Malondiamidine.*

By G. A. HOWARD, B. LYTHGOE, and A. R. TODD.

Some experiments have been made to examine the scope of the pyrimidine synthesis from esters and malondiamidine described by Kenner, Lythgoe, Todd, and Topham (J., 1943, 574). Present results suggest that it is of limited value for, although ethyl benzoate, ethyl oxalate, ethyl carbonate, and ethyl chloroformate condense to give pyrimidine derivatives, this does not appear to be the case with esters of a number of other acids examined.

4 : 6-*Diacetamido-2-methylpyrimidine* is formed in good yield when malondiamidine dihydrochloride is heated with a mixture of acetic anhydride and sodium acetate.

IN a previous communication (Kenner, Lythgoe, Todd, and Topham, J., 1943, 574) a synthesis of 4 : 6-diaminopyrimidine from ethyl formate and malondiamidine was described, and it was noted that by replacing the ethyl formate by ethyl acetate 4 : 6-diamino-2-methylpyrimidine could similarly be prepared. As this reaction of esters with malondiamidine represented a new synthesis of the pyrimidine ring system, it was desirable that the method should be further examined since it would, in theory at least, offer a means of preparing derivatives of 4 : 6-diaminopyrimidine bearing a variety of substituents in position 2. The purpose of this paper is to record the results of a brief survey of the applicability of the new synthesis. It is not claimed that a complete study of all the possibilities has been made, for our primary interest lay in the preparation of 2-substituted 4 : 6-diaminopyrimidines in which the group at position 2 would be of a type useful in our general scheme of nucleoside synthesis.

Despite the very ready reaction of ethyl formate and ethyl acetate, we were unable to isolate any pyrimidine derivative from the condensation of ethyl *n*-butyrate and malondiamidine, the major product of reaction being malondiamide. On the other hand, ethyl benzoate condensed as expected although the yield of 4 : 6-*diamino-2-phenylpyrimidine* was low. Ethyl carbonate reacted readily with malondiamidine to give 4 : 6-diamino-2-hydroxypyrimidine, and the same substance in the form of its *hydrochloride* was obtained when ethyl chloroformate was used. In the latter instance the chlorine atom appears to take part in the reaction rather than the carbonyl oxygen of the ester.

The case of ethyl oxalate was of interest since it seemed possible that it might react with 2 mols. of malondiamidine to give a tetra-aminodipyrimidyl. In fact no evidence for the formation of such a compound was obtained; only one of the ester groups reacted, the other being hydrolysed, and the sole product was 4 : 6-*diaminopyrimidine-2-carboxylic acid*, identified by decarboxylation to 4 : 6-diaminopyrimidine. No pyrimidine formation was observed when malondiamidine was heated with ethyl malonate, ethyl pyruvate, urethane, *N*-acetylurethane, phenylurethane or *NN*-dimethylurethane. In view of the greater reactivity of the dithio-acids than of the corresponding carboxylic acids, it was of interest to examine the behaviour of methyl dithioacetate; although this ester reacted readily enough with malondiamidine, only red resinous products were formed.

Although further work on a variety of esters would be necessary to make an accurate assessment of its value, it would appear from the experiments so far carried out that the synthetic method, although useful in certain cases, is of limited applicability.

The synthesis of pyrimidines by this method bears an analogy to the synthesis of triazines from esters and biguanide described by Rackmann (*Annalen*, 1910, **376**, 180). According to that author, a mixture of sodium formate and formic acid may be used in place of ethyl formate in the reaction with biguanide, and a mixture of acetic anhydride and sodium acetate may similarly replace ethyl acetate. Efforts on our part to prepare 4 : 6-diaminopyrimidine by heating malondiamidine or its dihydrochloride with a mixture of sodium formate and formic acid were unsuccessful, but with acetic anhydride and sodium acetate a crystalline product was formed in good yield. This proved to be 4 : 6-*diacetamido*-2-*methylpyrimidine*, identical with the compound obtained on acetylating 4 : 6-diamino-2-methylpyrimidine.

Experimental.

Ethyl Benzoate and Malondiamidine.—Malondiamidine dihydrochloride (20 g.; Kenner, Lythgoe, Todd, and Topham, *loc. cit.*) was added to a solution of sodium (6 g.) in methanol (100 c.c.), the precipitated sodium chloride removed, and the solution evaporated under reduced pressure. To the resinous diamidine thus obtained, ethyl benzoate (50 c.c.) was added, and the mixture warmed on the steam-bath for 1 hour, during which time the contents of the flask set to a greenish semi-solid mass. After standing overnight, this product was extracted (Soxhlet) with boiling absolute alcohol. The residue, largely sodium benzoate, was discarded, and the extract evaporated and subjected to vacuum sublimation. At 190°/10^{-3} mm. 4 : 6-*diamino*-2-*phenylpyrimidine* sublimed as colourless needles. Recrystallised from alcohol, it had m. p. 195—196° (Found : C, 64·5; H, 5·3; N, 30·2. $C_{10}H_{10}N_4$ requires C, 64·5; H, 5·4; N, 30·2%) (yield, 0·6 g.; 4%). The product was soluble in water and alcohol, but very sparingly so in common non-hydroxylic organic solvents; it appeared to be nitrosated (green colour) on treatment with sodium nitrite and dilute hydrochloric acid.

Ethyl Carbonate and Malondiamidine.—Ethyl carbonate (30 c.c.) was added to malondiamidine (prepared from 20 g. of dihydrochloride by the method described above), the mixture heated for 1 hour on the steam-bath, and left overnight. The pale green solid which had separated was collected and recrystallised from water (charcoal). Colourless needles (4 g.; 44%) were obtained which did not melt below 360° and showed the general reactions of the expected 4 : 6-diamino-2-hydroxypyrimidine (Found : C, 38·2; H, 4·9; N, 44·3. Calc. for $C_4H_6ON_4$: C, 38·1; H, 4·8; N, 44·2%).

Ethyl Chloroformate and Malondiamidine.—A solution of ethyl chloroformate (30 c.c.) in dry ether was added dropwise to malondiamidine (prepared from 20 g. of dihydrochloride). Violent reaction occurred during the addition, and after standing for 1 hr. the greenish solid was collected. On recrystallisation from water (charcoal), colourless needles (4 g.; 33%) of 4 : 6-*diamino*-2-*hydroxypyrimidine hydrochloride* were obtained (Found : C, 30·0; H, 4·8; N, 35·3; Cl, by Volhard titration, 21·8. $C_4H_7ON_4Cl$ requires C, 29·6; H, 4·3; N, 34·5; Cl, 21·8%). The substance had no m. p. and the free base had the reactions of the known 4 : 6-diamino-2-hydroxypyrimidine.

Ethyl Oxalate and Malondiamidine.—When ethyl oxalate (75 c.c.) was added to malondiamidine (prepared in the usual manner from 50 g. of the dihydrochloride) a violent reaction occurred with considerable evolution of heat. When it subsided the mixture was heated under reflux for 1 hour with dry ether (50 c.c.), and the solid product filtered off. Recrystallised from water, 4 : 6-*diaminopyrimidine*-2-*carboxylic acid* was obtained as colourless needles (50 g.) having no m. p. below 360° (Found : C, 38·3; H, 3·9; N, 35·6. $C_5H_6O_2N_4$ requires C, 38·9; H, 3·9; N, 36·4%). The acid dissolved readily in sodium carbonate solution. It was sparingly soluble in water, and aqueous solutions gave with ferrous sulphate a red precipitate insoluble in dilute nitric acid. Although it did not appear to be decarboxylated when heated with quinoline at 220° in presence of copper bronze, it lost carbon dioxide readily when warmed in a tube over a free flame. The decarboxylated material which sublimed had m. p. 263° and was identified as 4 : 6-diaminopyrimidine by its properties and by mixed m. p. with an authentic specimen.

4 : 6-*Diacetamido*-2-*methylpyrimidine.*—A mixture of malondiamidine dihydrochloride (20 g.), fused sodium acetate (20 g.), and acetic anhydride (150 c.c.) was refluxed for 5—6 hours, cooled, and filtered. The filtrate yielded acetamide on evaporation, and the residue, extracted (Soxhlet) with boiling alcohol, gave a solution which on cooling deposited 4 : 6-*diacetamido*-2-*methylpyrimidine*. Recrystallised from alcohol, this formed colourless needles (20 g.; 84%), m. p. 232°. In this form it was hydrated, the water of crystallisation being removed only by drying for more than 12 hours at 130°/1 mm. over phosphoric oxide (Found, in hydrated material : C, 47·8; H, 6·2; N, 25·3. $C_9H_{12}O_2N_4.H_2O$ requires C, 47·8; H, 6·2; N, 24·8%). The substance (1 g.) was hydrolysed by heating under reflux for 1 hour with sulphuric acid (10 c.c. of 70%), the resulting solution being diluted to 50 c.c., neutralised with barium hydroxide, filtered, and concentrated. 4 : 6-Diamino-2-methylpyrimidine separated, m. p. 298° undepressed by an authentic specimen.

For final identification, a small sample of 4 : 6-diamino-2-methylpyrimidine was refluxed with acetic anhydride and fused sodium acetate for 5 hours. The product was identical in m. p. and mixed m. p. with that obtained from malondiamidine as described above (Found : C, 47·4; H, 6·2; N, 25·3. Calc. for $C_9H_{12}O_2N_4.H_2O$: C, 47·8; H, 6·2; N, 24·8%).

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The University, Manchester. [*Received, May 30th*, 1944.]

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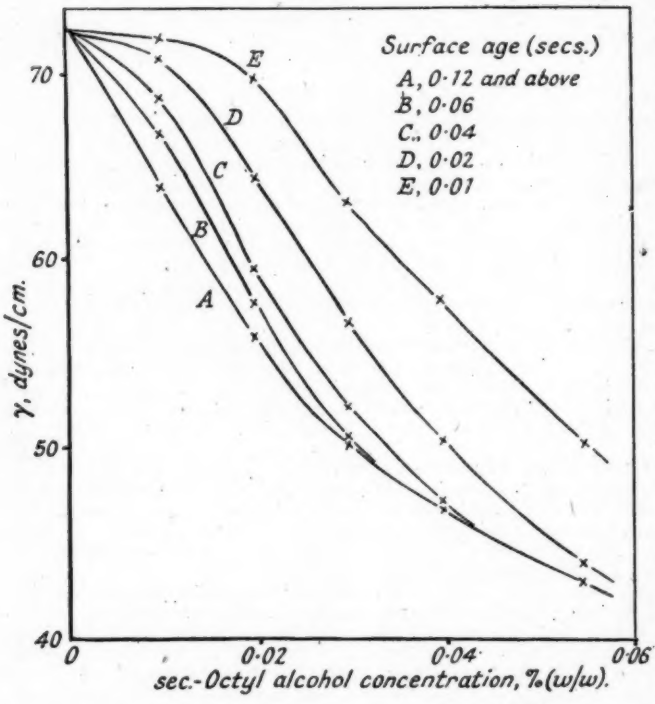
129. *The Properties of Freshly Formed Surfaces. Part III. The Mechanism of Adsorption, with Particular Reference to the* sec.*-Octyl Alcohol–Water System.*

By C. C. Addison.

Dynamic surface tensions of aqueous *sec.*-octyl alcohol solutions have been measured by the vibrating-jet method. The extent to which the free energy of the surface can be reduced by the adsorbate at any given concentration is shown to be the major factor controlling the velocity at which the adsorbate molecules migrate to the surface, and the variation in true velocity during adsorption has been determined.

THE vibrating-jet technique described in Part I (J., 1943, 535) was applied in Part II (this vol., p. 252) to the study of the dynamic surface tensions of aqueous solutions of *iso*amyl alcohol, and the mean velocity (termed the migrational velocity) at which molecules of *iso*amyl alcohol migrate from the bulk of the liquid to the surface was determined. The surface age at which equilibrium is established with this alcohol (of the order of 10^{-3} sec.) is so small, however, that the system could not be suitably applied to the study of true velocities of migration. Further work has shown that the range of surface ages available for measurement increases with increasing chain length. The upper limit is set by the solubility of the alcohol in water, which diminishes rapidly with increasing chain length, and the range of dynamic tensions (about 30 dynes/cm.) given by the lower members is not available beyond the C_8 alcohol. *sec.*-Octyl alcohol has been used in the present investigation, and dynamic surface tensions (obtained as shown in Part II) cover surface ages up to 0·12 sec. The results provide information on the variation in true velocity of migration to the surface, which takes place while adsorption is proceeding.

FIG. 1.



Migrational Velocity.—γ–c Curves for *sec.*-octyl alcohol solutions in water at 20° and at various surface ages are given in Fig. 1. The curves are similar in form to those already described for *iso*amyl alcohol. Curve A, which represents equilibrium conditions as determined by the vibrating jet, is in ideal agreement with that obtained by drop-weight measurements. The values of $d\gamma/dc$ obtained from this curve have been substituted in the approximate form of Gibbs's adsorption equation, $\Gamma = -c(d\gamma/dc)/\boldsymbol{R}T$, to obtain the maximum amount of adsorbate on the surface at each concentration (col. 3, Table I), it being assumed that, over the range of low concentration chosen, the activity coefficient of the solute does not differ appreciably from unity. By replotting the information in Fig. 1 to show directly the relation between γ and surface age, it is possible to determine the time required (t_1 seconds) for the establishment of equilibrium at each concentration; d (col. 4) represents the depth of solution from which the adsorbate is drawn. By employing the relationship given in Part II, *viz.*,

$$\text{Migrational velocity} = V = -100M(d\gamma/dc)/KTt_1$$

where $K = 83{\cdot}2 \times 10^6$ and M is the molecular weight of the alcohol, the values of V have been calculated (col. 6, Table I). It is to be emphasised that V represents the mean velocity of the migrating molecule, and is obtained directly from the maximum distance d travelled by the adsorbate molecules and the time t_1 required to establish equilibrium. It is therefore a useful index on which to compare rates of adsorption, and carries in itself no implication that the velocity is constant.

TABLE I.

c, %.	$-d\gamma/dc$.	$\Gamma \times 10^8$, g./cm.^{2}.	$d \times 10^5$, cm.	t_1, sec.	$V \times 10^4$, cm./sec.
0·01	800	4·30	43·0	0·120	36·0
0·02	640	6·90	34·5	0·095	36·2
0·03	490	7·90	26·5	0·070	37·6

The value of V for *sec.*-octyl alcohol is greater than that recorded in Part II for *iso*amyl alcohol (9×10^{-4} cm./sec.) and is again independent of concentration. The general relationship between V and chain length will be discussed more fully in a later part.

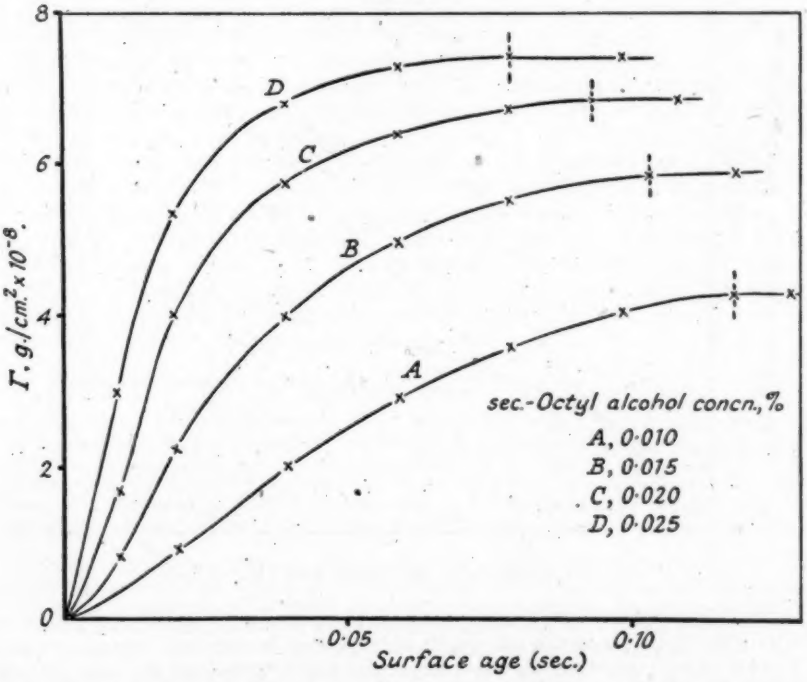
Factors controlling Velocity of Migration to the Surface.—The velocity of an adsorbate molecule migrating to a surface will be determined by a number of factors, including (*a*) the viscosity of the medium, (*b*) the dimensions and polar nature of the molecule, (*c*) the temperature, (*d*) the distance of the molecule from the surface, and (*e*) the free energy of the surface. The influence of the first three factors will vary with each particular case, but factors (*d*) and (*e*) have general application. Their relative significance can be deduced from the results given below.

In selecting the octyl alcohol system for study, the activity coefficient of the alcohol was not expected to deviate appreciably from unity in view of the very low concentrations required to produce large depressions in surface tension. In this case the more accurate form of Gibbs's equation, $\Gamma_2^{(1)} = -(\partial\gamma/\partial \log_e fc)/\boldsymbol{R}T$, where

f is the activity coefficient, could have been reduced to the above approximate form for the determination of velocities of migration throughout the available range of concentration. However, the mode of variation of $d\gamma/dc$ over the concentration range 0—0·06% (Curve *A*, Fig. 1) indicates that even in this system the activity coefficient deviates appreciably from unity at concentrations above 0·03%. Thus, when the equation $\Gamma = -c(d\gamma/dc)/\boldsymbol{R}T$ is applied to Curve *A*, Fig. 1, the value of Γ increases steadily up to a concentration of 0·03%, and the relation between γ and Γ is almost linear. Thereafter $d\gamma/dc$ falls more rapidly, and decreasing values of Γ are obtained. In the absence of values for the activity coefficients at the higher concentrations, calculation of Γ by the approximate form of Gibbs's equation has been restricted to the concentration range 0—0·03%. Under these conditions of extreme dilution, Γ will approximate closely to the amount of solute in a layer one molecule deep on the surface.

In determining the results in Fig. 2, the assumption has been made that a given value for γ represents a given Γ irrespective of surface age. The development of Γ with age of surface has been calculated on this basis

FIG. 2.



from the values in Fig. 1, and the results are given in Fig. 2 over the concentration range 0·01—0·025%. The broken vertical lines indicate the surface ages at which adsorption is complete. At any given surface age, the slope of the tangent to the curves in Fig. 2 represents the rate of arrival of adsorbate at the surface. 1 cm.² being taken as unit area of surface, the units of $d\Gamma/dt$ are in g./sec. These values are given in Table II, col. 4. The free energy of the surface with respect to the adsorbate molecules is defined for present purposes as the extent to which the surface tension can be lowered by accumulation of adsorbate at the surface. Thus if γ_t represents the surface tension at time t after formation of the surface, and γ_E represents the equilibrium value for that concentration, then the free energy of the surface is equal to $\gamma_t - \gamma_E$.

If the velocity of migration of adsorbate molecules is dependent upon the free energy, but is independent of distance from the surface, the value of $d\Gamma/dt$ should be proportional to $\gamma_t - \gamma_E$. If distance from the surface is a significant factor in determining velocity, this will not hold true. Values of $\gamma_t - \gamma_E$ are listed in Table II, col. 3, and the ratios are given in col. 5.

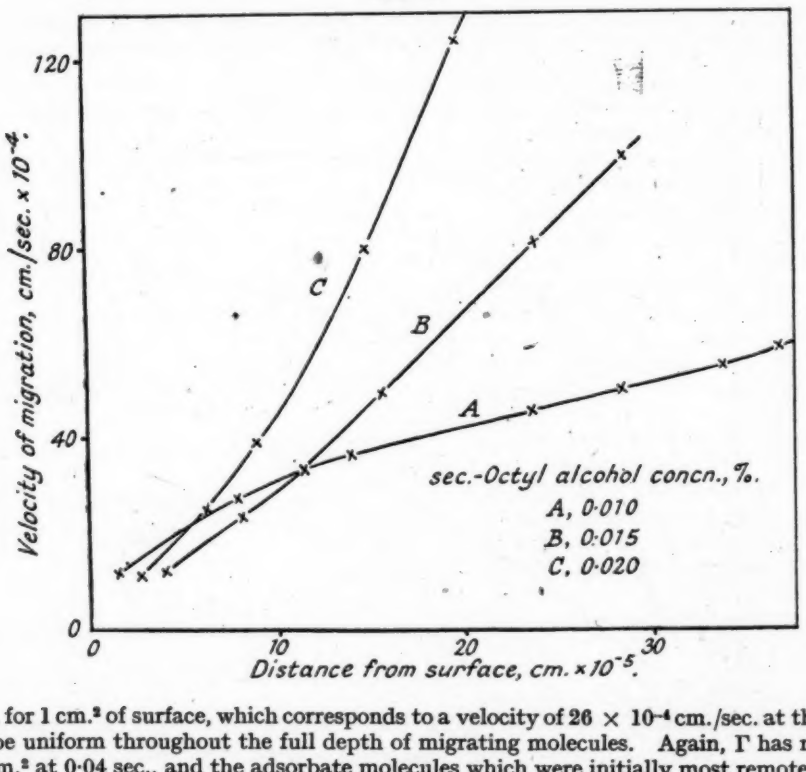
TABLE II.

c, %.	Surface age, sec.	$\gamma_t - \gamma_E$, dynes/cm.	$10^8 d\Gamma/dt$, g./sec.	$[10^8 d\Gamma/dt]/(\gamma_t - \gamma_E)$.
0·01	0·10	0·9	10·5	11·7
,,	0·08	2·1	25·0	11·9
,,	0·06	3·2	37·0	11·6
,,	0·04	4·4	46·5	10·6
0·015	0·07	1·3	16·3	12·5
,,	0·05	2·0	23·7	11·9
,,	0·03	4·9	51·3	10·5
0·02	0·08	0·8	11·5	14·4
,,	0·06	1·7	24·5	14·4
,,	0·04	3·5	52·0	14·9
,,	0·03	5·5	80·0	14·6

The ratios are sufficiently constant to indicate that free energy of surface is the major factor controlling migration velocity, and that distance from the surface is not significant. In view of the small velocities involved, and the high resistance to movement, the relative insignificance of the distance is feasible. The actual value of the ratio in Table II will be a function of concentration, and the above conclusions will hold true so long as the ratios are constant for any given concentration.

It is now possible to determine the actual velocities of the migrating molecules at any required distance from the surface. For example, at a concentration of 0·02%, solute is drawn from the bulk of the liquid to a depth of $34{\cdot}5 \times 10^{-5}$ cm. before an equilibrium surface layer is obtained. At a surface age of 0·04 sec., $d\Gamma/dt$ is

FIG. 3.



52×10^{-8} g./sec. for 1 cm.² of surface, which corresponds to a velocity of 26×10^{-4} cm./sec. at this concentration. This value will be uniform throughout the full depth of migrating molecules. Again, Γ has reached the value $5{\cdot}75 \times 10^{-8}$ g./cm.² at 0·04 sec., and the adsorbate molecules which were initially most remote from the surface will have advanced $28{\cdot}3 \times 10^{-5}$ cm., *i.e.*, they will be $6{\cdot}2 \times 10^{-5}$ cm. from the surface. This reasoning being used, results for three separate concentrations are recorded in Fig. 3. For each concentration, the curve given represents the variation in velocity of those adsorbate molecules most remote from the surface when adsorption commenced. The velocity of molecules at a distance smaller than d from the surface when adsorption commenced may be obtained by displacing the curve parallel to the distance axis to the required extent.

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130. *The Alkaloids of* Duboisia Leichhardtii.

By W. MITCHELL.

Duboisia Leichhardtii has been shown to contain hyoscyamine and small amounts of *l*-hyoscine, *dl*-hyoscine, norhyoscyamine, and a new alkaloid provisionally named "*Base D.*" The last was similar to but not identical with *iso*valeryltropëine, the *hydrobromide* of which has now been synthesised. The drug has been compared botanically with the *D. myoporoides* found not to contain hyoscyamine by Barger, Martin, and Mitchell (J., 1937, 1820; 1938, 1685). It is suggested that at least two distinct types of *Duboisia* have appeared in commerce.

IT was shown by Barger, Martin, and Mitchell (*locc. cit.*) that Australian *Duboisia myoporoides* yielded hyoscine, and small amounts of four new alkaloids, tigloidine, valeroidine, poroidine, and *iso*poroidine. Not one of the large number of samples which they examined showed any trace of hyoscyamine, this result being at variance with those of most of the earlier workers.

A specimen of Australian material offered on the market recently as "D. myoporoides" was found to contain 4·1% of total alkaloids, an unusually high figure. This product was fractionated, and the following

percentages of individual alkaloids were isolated: *l*-hyoscyamine, 1·97; *l*-hyoscine, 0·06; *dl*-hyoscine, 0·05; norhyoscyamine, 0·01; and a new alkaloid, 0·06, all expressed on the drug.

The drug showed no well-defined macroscopic differences from the *Duboisia* previously examined by Barger, Martin, and Mitchell, but only the dried leaves were available for examination: a comparison of the flowering specimens would probably have shown some characteristic differences. Dr. Metcalfe, of the Royal Botanic Gardens, Kew, very kindly undertook the botanical examination of the drugs. In the absence of flowering material this was rendered more difficult, but as a result of consideration of the stomatal distribution on the upper and the lower leaf surfaces it was possible to state with a fair degree of certainty that the material formerly found to contain no hyoscyamine was in fact authentic *D. myoporoides*, whereas the present specimen was probably *D. Leichhardtii*. Whatever the exact botanical distinction, the important point would appear to be that these two distinct types of *Duboisia*, and possibly other intermediate forms, have appeared on the market simply as "Duboisia" or "Duboisia myoporoides." This fact, which appears to be supported by recent work on *Duboisia* referred to in the Sixteenth Annual Report of the Council for Scientific and Industrial Research, Australia, for the year ended 30th June, 1942, would account for the discrepancies between the results of various investigators, and has almost certainly led to confusion in the past.

The new alkaloid, $C_{13}H_{23}O_2N$, referred to above was similar to tigloidine, valeroidine, and the poroidines in that its *hydrobromide* was very soluble in chloroform. It was optically inactive and saturated. On hydrolysis it yielded tropine and a liquid acid thought to be a valeric acid. It was not possible to identify this latter with certainty, but it is probably mainly *iso*valeric acid. iso*Valeryltropëine hydrobromide* was synthesised but was not identical with the above hydrobromide. It is quite possible, as in the case of "Base Z," which was later shown to consist of a mixture of the isomers, poroidine and *iso*poroidine (*ibid.*), that this material is also an isomeric mixture, but owing to the very small amount of material available it was not possible to pursue the matter further. Since its constitution is thus not definitely established it is suggested that the material be identified by the name "*Base D*". It is of interest to note that whereas *D. myoporoides* yielded minor alkaloids which were esters of ψ-tropine, a dihydroxytropane, and nortropine respectively, *D. Leichhardtii* has yielded a minor alkaloid which is an ester of tropine, and that except in the case of tigloidine, which was tiglyl-ψ-tropëine, they were all pentoic acid esters.

Experimental.

Isolation and Separation of the Alkaloids.—The drug (No. 20 powder) was extracted with cold alcohol, and the total alkaloids isolated by the usual methods. They were converted into hydrobromides, and the solution concentrated, but no crystalline material could be isolated. The hydrobromides were then converted into neutral oxalates, and the solution concentrated. Partly racemised hyoscyamine oxalate (29 g.), m. p. 190° (corr.), was separated. The mother-liquor would not yield any further crystalline material, and small amounts were therefore converted severally into hydrobromide, sulphate, neutral phosphate, borate, picrate, and *d*-camphorsulphonate. None of these solutions crystallised after concentration.

The various solutions were united, basified with ammonia, and the alkaloids extracted with chloroform. The chloroformic solution was fractionally extracted with aqueous N-oxalic acid, and the various fractions concentrated. These all crystallised, and yielded a total of 19·5 g. of partly racemised hyoscyamine oxalate, m. p. ranging from 188° to 194° (corr.). By repeated refractionation of the mother-liquors from this material, a further quantity of 13·5 g. was obtained, making a total of 62 g., equivalent to 1·97% of hyoscyamine alkaloid on the drug. In addition, 0·35 g. of an oxalate, m. p. 227—228° (corr.), was separated; this was norhyoscyamine oxalate (see below).

The final mother-liquors from the oxalates were united, basified with ammonia, and the alkaloids extracted with chloroform and converted into hydrobromides. The concentrated solution was extracted with two portions of chloroform (15; 15 ml.). The residue from the chloroform slowly crystallised, and the crystals were collected and washed with acetone; this was "*Base D*" *hydrobromide* (see below).

The aqueous solution of the hydrobromides so extracted was concentrated and chilled. Crystals (2·3 g.), m. p. 184° (corr.), separated. Further concentration of the mother-liquor yielded a second crop (1·9 g.), m. p. 167° (corr.); these were respectively the hydrobromides of *l*-hyoscine and *dl*-hyoscine (see below).

Purification of the Separate Alkaloids.—Hyoscyamine. The various fractions of partly racemised hyoscyamine oxalate were dissolved in water, basified with ammonia, and the alkaloid extracted with chloroform. After racemisation by the addition of a small amount of sodium hydroxide to its cold alcoholic solution (Will, *Ber.*, 1888, **21**, 1723), the alkaloid was converted into hydrobromide. The resultant material crystallised from alcohol–acetone in opaque white nodules, m. p. 163·5° (corr.) not depressed by authentic atropine hydrobromide (Found: C, 55·3; H, 6·2; N, 3·9; Br, 21·0. Calc. for $C_{17}H_{23}O_3N,HBr$: C, 55·1; H, 6·5; N, 3·8; Br, 21·6%).

Norhyoscyamine. The oxalate, m. p. 227—228° (0·35 g.), was repeatedly recrystallised from acetone containing a trace of water and thereby obtained in felted needles, m. p. 249° (corr.) [Found: C, 63·2; H, 6·5; N, 4·6. Calc. for $(C_{16}H_{21}O_3N)_2,H_2C_2O_4$: C, 63·7; H, 6·9; N, 4·4%]. No authentic material was available for comparison.

Hyoscine. Each of the two crops of hydrobromide obtained was recrystallised first from alcohol–ether and then from water; in each case colourless, efflorescent prisms were thereby obtained: From first crop, m. p. 195—196° (corr.) not depressed by authentic *l*-hyoscine hydrobromide (Found: C, 46·9; H, 6·3; N, 3·2; Br, 18·3. Calc. for $C_{17}H_{21}O_4N,HBr,3H_2O$: C, 46·6; H, 6·4; N, 3·2; Br, 18·3%); $[\alpha]_D^{20°}$ −24·4° (*c*, 5·0 of anhydrous salt in water). From second crop, m. p. 185° (corr.) not depressed by authentic *dl*-hyoscine hydrobromide (Found: N, 3·2; Br, 18·4. Calc. for $C_{17}H_{21}O_4N,HBr,3H_2O$: N, 3·2; Br, 18·3%); it was optically inactive (*c*, 5·0 of anhydrous salt in water).

"Base D." The *hydrobromide* crystallised from dry acetone in glistening plates, m. p. 231° (corr.) depressed to *ca.* 205° by tigloidine hydrobromide (m. p. 234—235°) with which it was at first thought to be identical (Found: C, 50·6; H, 7·6; N, 4·6; Br, 26·0. $C_{13}H_{23}O_2N,HBr$ requires C, 51·0; H, 7·8; N, 4·6; Br, 26·1%); it was optically inactive (*c*, 8·0 in water), and very soluble in chloroform, water, and alcohol.

Hydrolysis of "Base D."—The base from 0·4 g. of hydrobromide was boiled for 2 hours with barium hydroxide (0·75 g.) in water (10 ml.). After removal of the barium as sulphate, the acid filtrate was extracted with ether, which left 0·09 g. of an oily acid with a powerful odour of valeric acid; yield, 68%. The *p*-phenylphenacyl ester, m. p. 78° (corr.), formed dull, colourless laminæ from 60% alcohol. The m. p. was depressed to *ca.* 68° by mixing with an equal weight of

the ester (m. p. 76°) of *iso*valeric acid and differs from those of the other three isomeric esters; the material is possibly a mixture of two of these. *p*-Phenylphenacyl tiglate was made for comparison and formed glistening laminæ, m. p. 104—105° (corr.).

The solution from which the valeric acid had been extracted was neutralised with sodium hydroxide and concentrated (5 ml.). It was basified with an equal volume of 50% aqueous sodium hydroxide solution and repeatedly extracted with chloroform. The residue from the chloroform was boiled for 1 hour with acetic anhydride (5 ml.), and the product isolated and purified in the usual manner. Colourless, prismatic needles were thus obtained (from alcohol–ether), m. p. 188° (corr.) not depressed by authentic acetyltropëine hydrobromide, but depressed to 145° by acetyl-ψ-tropëine hydrobromide (m. p. 205°).

Synthesis of iso*Valeryltropëine Hydrobromide.*—Tropine (2·8 g.) was titrated with hydrochloric acid and the solution evaporated in a vacuum: Tropine hydrochloride so obtained was esterified with *iso*valeryl chloride (3 g.), and the product isolated and purified as in the case of tigloidine (*loc. cit.*). It formed colourless, pearly plates from alcohol–ether, and was extremely soluble in water, chloroform, and alcohol, but insoluble in ether, and was deliquescent (Found: C, 51·1; H, 7·7; N, 4·6; Br, 25·9. $C_{13}H_{23}O_2N,HBr$ requires C, 51·0; H, 7·8; N, 4·6; Br, 26·1%); m. p. 225—227° (corr.) depressed to *ca.* 200° by " Base D " hydrobromide; yield 60%.

My thanks are due to Messrs. T. and H. Smith, Ltd., Edinburgh, for supplies of material, to Wm. F. Martin, Esq., F.R.I.C., for his continued interest and advice, and to The Royal Botanic Gardens, Kew, for the botanical examination of the drugs.

Laboratories of Messrs. T. & H. Smith, Ltd., Edinburgh. [*Received, May 17th*, 1944.]

NOTE.

The Preparation of m-*Nitrobenzenesulphonyl Chloride.* By Herbert H. Hodgson and John S. Whitehurst.

The directions for making this compound from nitrobenzene and chlorosulphonic acid given in D.R.-P. 89,997 (cf. Friedländer, 1894—1897, IV, pp. 38—39) are insufficient for obtaining consistent results on a laboratory scale, and the following more detailed description has been found satisfactory: Dry nitrobenzene (123 g., 1 g.-mol.) and chlorosulphonic acid (350 g., 3 g.-mols.) are stirred together at room temperature until thoroughly mixed (any temperature rise indicates water in the nitrobenzene), the temperature is then raised gradually to 100°, maintained there for 2 hours, and thereafter kept at 110—120° for 6 hours. The initial yellow colour has now changed to brown and the reaction is completed by a final heating at 125—130° for 2 hours, *i.e.*, a total heating period of 10 hours. After cooling, the solution is poured into a mixture of ice (1 kg.) and water (1 kg.), and the white precipitate collected, washed with water, and air-dried. Yield, 170 g. (76% of the theoretical); m. p. 54°. The crude *m*-nitrobenzenesulphonyl chloride is purified by dissolution in glacial acetic acid (500 c.c.), the filtered solution cooled below 15° (otherwise dilution with water precipitates the compound as a semi-fused mass), and water (200 c.c.) added cautiously with stirring; *m*-nitrobenzenesulphonyl chloride then separates in colourless prismatic needles, which are washed with 50% acetic acid and air-dried; m. p. 62° (Armstrong, Colgate, and Rodd, *Proc. Roy. Soc.*, 1914, [*A*], **90**, 111, give m. p. 61·5—62°). Yield of purified product, 124 g. (55%).

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